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Endovascular Correction of an Acquired Left Ventricular to Right Atrial Communication **Following Surgical Correction** of Transposition of the Great Arteries in a Child (A Clinical Case) V.N. Ilyin, A.G. Osiev, E.Yu. Danilov, V.A. Kryukov, O.Yu. Kornoukhov, A.A. Valitova, O.I. Kalinina **p. 25**

ECMO in Urgent Percutaneous Coronary Intervention in a Patient with AMI **Complicated by Cardiogenic**

A.G. Osiev, V.I. Baystrukov, A.V. Biryukov, O.V. Krestyaninov, D.A. Redkin, I.A. Kornilov, E.I. Kretov **p. 37**

Coronary Heart Disease in Patients with Diabetes Mellitus: **Possibilities and Perspectives** of Interventional and Surgical Treatment (Literature Review) A.V. Kulikov, E.V. Yarnykh, V.S. Chekanov **p. 48**





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Contents

INTERVENTIONAL RADIOLOGY

| The Choice of Endovascular Intervention on the Iliac Arteries for the Hybrid Operations in Patients with Multilevel Atherosclerotic Lesions of the Lower Limb Arteries |
|---|
| A.V. Troitskiy, A.G. Bekhtev, R.I. Khabazov, G.A. Belyakov, E.R. Lysenko, V.S. Skrubert, O.G. Gryaznov, A.S. Azaryan, E.D. Solov'eva, I.M. Zakharova |
| INTERVENTIONAL CARDIOLOGY |
| Outcomes of the Invasive Treatment in Women with Coronary Heart Disease |
| A.B. Shames, V.A. Ivanov |
| Results of Endovascular Treatment of Patients with Non-Q Wave Myocardial Infarction A.A. Filatov, V.V. Krylov |
| INTERVENTIONAL CARDIOLOGY AND CARDIAC SURGERY |
| Endovascular Correction of an Acquired Left Ventricular to Right Atrial Communication Following Surgical Correction of Transposition of the Great Arteries in a Child (A Clinical Case) <i>V.N. Ilyin, A.G. Osiev, E.Yu. Danilov, V.A. Kryukov,</i> <i>O.Yu. Kornoukhov, A.A. Valitova, O.I. Kalinina</i> |
| CLINICAL CARDIOLOGY |
| The Association Between Chronic Ischemic Mitral Regurgitation and the Localization of Coronary Stenoses in Patients with Postinfarction Cardiosclerosis |
| V. A. Kuznetsov, E.I. Yaroslavskaya, I.P. Zyryanov, G.S. Pushkarev, D.V. Krinochkin, L.V. Marynskikh |
| MISCELLANEOUS |
| ECMO in Urgent Percutaneous Coronary Intervention in a Patient with AMI Complicated by Cardiogenic Shock |
| A.G. Osiev, V.I. Baystrukov, A.V. Biryukov, O.V. Krestyaninov, D.A. Redkin, I.A. Kornilov, E.I. Kretov |
| REVIEWS |
| Peculiarities of the Clinical Course of an Acute Myocardial Infarction with Non-Occlusive Lesion of the Infarct-Related Artery (Literature Review) O.V. Simonov, I.Yu. Kostyanov, A.G. Koledinsky, P.S. Vasillev, D.S. Kurtasov |
| Coronary Heart Disease in Patients with Diabetes Mellitus: Possibilities and Perspectives of Interventional and Surgical Treatment (Literature Review) |
| A.V. Kulikov, E.V. Yarnykh, V.S. Chekanov |

The Choice of Endovascular Intervention on the Iliac Arteries for the Hybrid Operations in Patients with Multilevel Atherosclerotic Lesions of the Lower Limb Arteries

A.V. Troitskiy^{*}, A.G. Bekhtev, R.I. Khabazov, G.A. Belyakov, E.R. Lysenko, V.S. Skrubert, O.G. Gryaznov, A.S. Azaryan, E.D. Solov'eva, I.M. Zakharova Clinical Hospital N119, Center for Cardiovascular and Endovascular Surgery, Khimki, Moscow region, Russia

We analyzed the immediate and long-term outcomes of hybrid surgeries for multilevel atherosclerotic lesions of aortoiliac and femoropopliteal segments. The clinical material comprises 221 patients with multilevel lesions of the iliac arteries and the lower limb arteries, classified as TASC A, B, C and D. Loop endarterectomy from iliac arteries combined with stenting is described as a method of choice in patients from the risk group for concomitant pathology with TASC C and D lesions of the iliac arteries. Recommendations on reducing the number of complications and on improving the long-term outcomes are given, including conduction of preventive surgeries in the late follow-up period.

Key words: loop endarterectomy, hybrid surgeries, stenting of the iliac arteries.

Objective. To determine the optimal techniques for endovascular intervention on the iliac arteries during hybrid surgeries in patients with multilevel atherosclerotic lesions of the lower limb arteries.

Materials and methods. Since 1997 till 2012, 221 patients with multilevel lesions of the iliac arteries and the lower limb arteries (TASC A, B, C and D) have undergone hybrid surgeries at Clinical Hospitals N83 and N119 of the Federal Biomedical Agency of Russia. All surgeries were performed simultaneously. The patients were divided into groups according to the type of intervention on the iliac arteries: 1 balloon angioplasty of the iliac arteries; 2 stenting of the iliac arteries; 3 - loop endarterectomy from the iliac arteries with subsequent implantation of uncoated stent into the region of intimal cylinder rupture. The following reconstructions of femoropopliteal segment were performed in all the groups: common femoral artery endarterectomy (CFA EAE), profundoplastics, femoral proximal popliteal (FpPB) and femoral distal popliteal bypass surgery (FdPB), as well as femorotibial bypass surgery (FTB).

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Results. Technical success rate was 99.1%. Intraoperative complications which required conversion were observed in 2 cases. Immediate postoperative complications affecting the patency of conducted reconstructions were registered in 10 patients (4.5%). Iliacofemoral vascular replacement was performed in 3 patients within 1 to 8 days due to thrombosis of the iliac arteries; 2 patients required additional implantation of stents into the iliac arteries within the same time frame due to dissections detected by ultrasound duplex scanning. Also, thromboses of femoropopliteal bypasses occurred in 5 cases; they required thrombectomy. Thus, the patency, deducting the cases of technical failure, was 98.6% at in-hospital stage. The long-term outcomes were followed up for 5 years in 76.5% of patients. Five-year assisted primary patency of the aortoiliac region was as follows: 70.2% in Group 1; 77.9% in Group 2; 89.4% in Group 3. Patency outcomes significantly differed between Groups 1, 2 and 3. Five-year cumulative patency of the femoropopliteal segment was as follows: 98.2% for CFA EAE, 100% for profundoplastics, 77.3% for FpPB; 74.1% for FdPB; 61.4% for FTB. No significant differences were registered in the patency of femoropopliteal reconstructions, depending on the type of intervention in the aortoiliac segment.

Introduction

The spreading of atherosclerosis results in an increased number of patients, including

The Choice of Endovascular Intervention on the Iliac Arteries for the Hybrid Operations in Patients with Multilevel Atherosclerotic Lesions of the Lower Limb Arteries

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those with lesions of aorta, iliac arteries and the lower limb arteries. Thus, combined arterial lesions of aortoiliac and femoropopliteal segments make up to 91% of all cases of peripheral atherosclerosis, according to the data of various authors (1). Precisely multisegmental lesions of the lower limb arteries maximally reduce the blood flow and often cause the critical lower limb ischemia, and so far the treatment of patients with multilevel atherosclerotic lesions has been one of the most tactically complicated tasks of angiology and vascular surgery (2, 3).

Until recently, open arterial reconstructions were the leading methods for the restoration of patency of the iliac arteries and the lower limb arteries. However, the long-term patency of proximal reconstructions in patients with multisegmental lesions is significantly inferior to that in patients with uncompromised outflow tracts. A number of studies confirmed that exactly the condition of outflow tracts is the primary factor affecting the long-term outcomes of aortoiliac reconstructions (4). However, considering the fact that up to 90% of patients with obliterative arterial diseases of the lower limbs are at an increased surgical risk due to the concomitant pathology, the use of multisegmental open surgical reconstructions has substantial limitations. Moreover, the perioperative mortality rate for bypass surgeries of the aortoiliac segment alone reaches 2 - 4%, and the number of complications is up to 25% (5).

Endovascular techniques for correction of the aortoiliac arteries make it possible to avoid a large number of complications, and the longterm patency comparable with open surgical reconstructions is demonstrated in a number of cases. However, the use of such techniques in treatment of femoropopliteal lesions gives significantly worse long-term outcomes compared with bypass surgeries (6).

Endovascular techniques for restoration of the blood flow combined with open reconstructive surgeries (so called hybrid surgery) achieve maximal hemodynamically significant results in treatment of patients with multisegmental lesions. Due to simultaneous correction of both inflow and outflow vessels, the longterm patency outcomes are improved for each reconstruction, as compared with the isolated correction of one segment (7-9).

However, until now there have been some unsolved issues in the hybrid surgery of the multifocal atherosclerosis, such as indications for the hybrid surgeries, timing and sequence of the various stages, and the long-term outcomes. Restrictions for the use of endovascular stage in patients with severe TASC C and D lesions of the inflow arteries are also an important issue, and this significantly complicates the treatment of such patients (10, 11).

Material and methods

We present our experience with surgical treatment of 221 patients with obliterating atherosclerosis who underwent 221 hybrid surgeries, involving endovascular intervention on the iliac arteries in combination with the open surgical reconstruction of the femoropopliteal arteries.

The patients were assigned to three groups.

Group 1: 31 patients who underwent balloon angioplasty of the iliac arteries with an open distal reconstruction.

Group 2: 150 patients who had stenting of the iliac arteries with an open distal reconstruction.

Group 3: 40 patients who underwent loop endarterectomy from the iliac arteries with subsequent stent implantation into the region of intimal cylinder rupture in combination with an open distal reconstruction.

The type and ration of performed distal reconstructions were comparable between the groups.

The following reconstructions of the femoropopliteal segment were performed:

• Endarterectomy from the common femoral artery with patch repair in 47 patients.

• Profundoplastics in 43 patients.

• Femoral proximal popliteal bypass surgery in 89 patients.

• Femoral distal popliteal bypass surgery in 26 patients.

• Femorotibial bypass surgery in 16 patients. 95% of patients were males. The age of patients varied in the range of 62.6 ± 6.5 years. Disease duration was 3.4 ± 3.87 years. Concomitant pathology was observed in 204 out of 221 patients (92.31%).

Aortoiliac segment lesions were classified as follows:

- TASC A 63;
- TASC B 103;
- TASC C 37;
- TASC D 18 patients.

Meanwhile, TASC-A lesions were observed in Group 1 in the vast majority of cases (67.7%); 62.7% of patients in Group 2 had TASC-B lesions; and 100% of lesions in Group 1 were TASC-C and TASC-D lesions. Femoropopliteal lesions showed comparable patterns in all three



Figure 1. Distribution of aortoiliac arterial lesions in the groups of study.



Figure 2. Distribution of femoropopliteal arterial lesions in the groups of study.

groups, and in the general cohort the pattern was as follows:

- TASC A 32;
- TASC B 67;
- TASC C 96;
- TASC D 26 patients.

The distribution of arterial lesions of aortoiliac and femoropopliteal segments within the groups according to TASC classification is presented in Figure 1 and 2.

Patients with combined arterial lesions of aortoiliac and femoropopliteal segments were

comprehensively examined, including primary examination, medical history and local status. Complex instrumental examination included ultrasound dopplerometry, color-flow duplex scanning and X-ray angiography. Each of the above methods provides specific information, which, if combined, allows a surgeon to see the whole picture, both in terms of the lesion type and the functional state of regional hemodynamics in the limb.

The most important issue of surgery is the determination of indications for surgical inter-

vention. The sequence and the order of conducting hybrid surgeries has been the topic for discussion to date. Uniform guidelines regarding most lesions are not published yet; therefore, in our work we used guidelines of the Transatlantic Inter-Society Consensus (TASC II -Inter-Society Consensus for the Management Peripheral Arterial Disease of 2007). Considering the fact that these guidelines review isolated lesions of individual segments, the type of intervention on each particular segment during hybrid surgeries is determined according to the guidelines on revascularization of the relevant TASC II lesion.

As for timing of the surgery stages, we think that the highest results may be obtained when performing the stages simultaneously, which is confirmed by a number of authors.

Thus, for aortoiliac TASC- A and TASC-B lesions in Groups 1 and 2 of our study, an open reconstruction was initially conducted on the femoropopliteal arteries; after that, endovascular intervention on the aortoiliac arteries was performed. Endovascular intervention included balloon angioplasty or stenting of the iliac arteries using a standard procedure. In our opinion, such an approach has a number of benefits: the puncture of femoral artery is not required if there is a direct access to the lumen of femoral artery, and the vessel wall is therefore less traumatized, with less complications related to such trauma. Also, the incidence of thrombosis in the angioplasty region is decreased as there is no need in the long-term cross-clamping of the femoral arteries, which would have been necessary in case of further reconstruction on the infrainguinal arteries.

These guidelines inevitably lead to difficulties when treating patients with multilevel TASC- C and D lesions. Exactly combinations of TASC -C and D lesions of the iliac arteries with femoropopliteal arterial lesions are considered to be contraindications for hybrid surgeries by most authors. However, this category of patients most frequently have severe multifocal atherosclerosis and multiple concomitant pathologies, so the perioperative risk and the number of complications increase manyfold. Besides, surgical correction of only one segment almost never results in adequate regress of ischemia.

We used loop endarterectomy from the iliac arteries with subsequent implantation of the stent into the region of intimal cylinder rupture in combination with an open distal reconstruction in this category of patients for the treatment of aortoiliac lesions. Therefore, there was no need for endovascular intervention on the common femoral artery and on the distal segments of the external iliac artery. The sequence of conducting the surgery stages was the opposite in Group 3 as compared with the first two groups. Preconditions for performing initial intervention on the aortoiliac arteries are as follows: combined lesions of the iliac arteries and the common femoral artery; technical peculiarities of the intervention itself and also an increased risk of conversion in case of complications during the endovascular stage. The technique involved compulsory threading of stenoocclusive lesions in the iliac arteries by a guide wire, replacement of a guide wire by an extra-stiff 0.035 guide wire, loop endarterectomy using a guide wire under fluoroscopic guidance, and implantation of the stent into the region of intimal cylinder rupture.

The stages of surgery are shown in Figures 3–7.

Results of the study

Technical success was achieved in 99.1% (219 patients) out of 221 hybrid surgeries. Intraoperative complications that required conversion were observed in 2 cases. Intraoperative complications in 6 more cases (2.7%) resulted in changing of the initial surgical plan. No fatal outcomes were observed. Intraoperative complications developed in 6 patients (2.7%) during the endovascular stage and in 2 patients during the open surgery stage. They included migration and dislocation of stents, extended dissections of the iliac arteries and aorta, perforation of iliac artery walls. A case of a similar complication is presented in Figures 8-10. Complications were managed by using endovascular techniques (implantation of additional stents or stent grafts) in 4 cases, and 2 more cases (0.9%) required conversion. Complications of open surgical reconstructions included intraoperative thromboses of femorotibial bypasses due to compromised distal lumen. Satisfactory long-term outcomes were achieved in 1 case due to bypass distalization.

Immediate outcomes of the surgeries were considered to be +2 and +3 in 220 patients, and 0 in 1 patient according to the Rutherford scale of changes in a clinical status.

Different postoperative complications were observed in 35 patients (15.8%). Complications affecting the patency of conducted interventions were observed in 10 patients (4.5%), local complications that do not affect the patency of reconstructions – in 22 patients



Figure 3. Angiogram at baseline. Occlusion of the right external iliac artery.



Figure 4. Passage of the lesion with a guidewire under X-ray guidance.



Figure 5. Performing loop endarterectomy from the right external iliac artery using a guidewire under X-ray guidance.



Figure 6. Stent implantation into the area of intimal cylinder rupture.



Figure 8. Angiogram at baseline. Stenosis of the right external iliac artery.

Figure 7. Final angiogram.



Figure 9. Angiogram after failed endaterectomy. An extensive dissection of the iliac arteries and terminal aortic segment is seen.



Figure 10. Final angiogram after stenting of the common and external right iliac arteries and stent-grafting of the terminal aorta.



Figure 11. Primary assisted patency of the iliac arteries in different groups.

(9.9%) and common postoperative complications – in 3 patients (1.4%).

A high rate of primary success in Group 3 in combination with a low number of intraoperative complications became possible due to the modified technique of iliac artery loop endarterectomy. Advancement of the loop using an extra-stiff 0.035 guide wire is an important step which is conducted under fluoroscopic control. The advantage of the stiff guide wire is that it straightens the iliac arteries and serves as a good support for the loop. Fluoroscopic control, in its turn, allows us to measure out an effort for advancing the loop, which is extremely important in calcinoses and rigid stenoses. This technique takes into consideration arterial deformation, thus lowering the possible risk of perforation.

The long-term outcomes were followed up in 76.5% patients (169 out of 221 patients). Mean follow-up was 51 ± 14.5 months.

Ten persons (4.5%) died in the late follow-up period within different time frames after the surgical intervention due to the causes not related to the earlier conducted surgery.

None of the followed patients underwent large amputations during the late postoperative period.

We assessed the primary patency of both segments, and also the primary assisted patency of the aortopopliteal segment and the cumulative patency of the femoropopliteal segment in all three groups.

The primary five-year patency of the aortoiliac segment was 42.5% in Group 1, 57.2% in Group 2 and 62% in Group 3.

Five-year primary assisted patency was 70.2% in Group 1, 77.9% in Group 2 and 89% in Group 3. The diagram representing the primary assisted patency of the iliac arteries is shown in Figure 11.

There were no statistically significant differences in the primary patency between three groups. However, this fact should be interpreted considering that only patients with TASC C and D lesions underwent interventions in Group 3, and the obtained results are significantly comparable with the results of endovascular interventions for TASC A and B lesions.

In-stent restenoses of the iliac arteries (restenoses in the region of balloon angioplasty if balloon angioplasty was performed) had



Figure 12. Cumulative patency of reconstructed femoropoplital segment in different groups.

the main impact on reducing the primary patency. In total, they were registered in 19 patients (8.6% out of all study patients). Balloon angioplasty had significantly worse outcomes as for incidence of restenoses in the region of primary intervention compared with using stents.

Also, *de novo* stenoses of the regions in the iliac arteries which were not earlier exposed to interventions had a great impact on reducing the primary patency in Groups 1 and 2. They were observed in 11 patients (5.0%). De novo stenoses affected the primary patency of the aortoiliac region mainly after a 3-year follow-up period.

lliac artery thromboses were diagnosed in 7 patients (3.2%) during the five-year follow-up period. No significant differences were revealed in the incidence of thromboses, depending on the type of intervention on the iliac arteries.

Reduction of the primary patency in Group 3 was caused by slightly different factors than in the first two groups. No cases of iliac artery de novo stenoses were detected throughout the whole follow-up period in Group 3, which is explained by the maximally complete vessel desobliteration with a removal of an affected intima almost along the whole length of the ves-

sel. However, the blood flow obstacles, such as flotation of intima on the edge of the earlier implanted stent, were observed in the late follow-up. All patients with intimal flotation received stents less than 2 cm long. Apparently, it was impossible to completely overlap the floating intima by the short stent, despite satisfactory angiographic results. Eventually, considering the obtained data, we started using stents not shorter than 4 cm during later work stages, and we did not observe any cases of intima flotation in the late period.

When comparing the primary patency outcomes depending on the region of intervention, the best parameters were observed in a group of patients who underwent isolated stenting of the common iliac artery. The worst results were obtained during simultaneous stenting of common and external iliac arteries, while stenting of the common iliac artery had shown intermediate results.

Five-year primary patency of femoropopliteal reconstructions was as follows: 98.2% for endarterectomy of the common femoral artery with plastics; 89% for profundoplastics; 60% for femoral proximal popliteal bypass surgery; 56.5% for femoral distal popliteal bypass surgery; 36% for femorotibial bypass surgery. Five-year cumulative patency was as follows: 98.2% for CFA EAE, 100% for profundoplastics,77.3% for FpPB, 74.1% for FdPB, 61.4% for FTB. The diagram representing the cumulative patency is shown in Figure 12. There were no significant differences between the primary and cumulative patency of femoropopliteal reconstructions, depending on the type of intervention on the aortopopliteal segment. This suggests that an adequate correction of inflow arteries ensures the normal functioning of distal reconstructions, and any patency reduction in the aortoiliac segment negatively affects the patency of femoropopliteal segment.

When assessing effects of the inflow arteries patency on the patency of distal reconstructions, the long-term patency of femoropopliteal reconstructions turned out to be statistically significantly higher as long as there were no long-term significant hemodynamic alterations in the aortoiliac arteries.

Preventive surgeries on the aortoiliac segment preclude from reduction of patency in both segments under reconstruction. Moreover, it is important that the overwhelming majority of preventive surgeries on the aortoiliac segment were endovascular.

Compulsory ultrasound duplex scanning every 6 months after the initial surgery can detect most restenoses, and necessary preventive surgery can be performed promptly. Moreover, compulsory check-ups in the late follow-up period can help to control *de novo* stenoses.

Conclusions

Thus, we have come to conclusion that hybrid surgeries for multilevel atherosclerotic lesions of aortoiliac and femoropopliteal seqments achieve optimal results in revascularization of the limb. Simultaneous removal of some hemodynamic blocks on different levels leads to a complete regress of ischemia in nearly all patients. The use of iliac artery loop endarterectomy with stenting allows simultaneous hybrid reconstructions in patients with TASC C and D lesions. Reduction of surgical trauma during the hybrid surgeries as compared with simultaneous two-level surgical reconstruction, as well as the possibility to conduct interventions using regional anesthesia, is especially important in patients at high risk of complications due to concomitant pathology.

Right indications, proper use of each technique and adequate extent of the surgery result in good immediate and long-term outcomes. Timely diagnostics of late complications (via mandatory duplex scanning in the late followup period) also underlies the success. For ensuring the best long-term outcomes, an active surgical tactics regarding preventive surgeries is also of importance.

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Outcomes of the Invasive Treatment in Women with Coronary Heart Disease

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According to the published data, female gender is a risk factor for invasive treatment of coronary heart disease (CHD) due to anatomical and pathological features. The analysis of the efficacy of coronary angioplasty with stenting was performed in 284 women with different CHD types. In the authors' opinion, invasive treatment is a method of choice in women with CHD at high cardiac risk.

Key words: coronary hearth disease in women, invasive treatment.

Introduction

Coronary heart disease (CHD) has been considered, for a long time, a disease usually typical for middle aged males. Currently, in economically developed countries worldwide CHD is the leading reason of death in elderly and old women (11). In the USA, more than 500,000 women die annually from cardiovascular diseases; one-year mortality rates after confirmed myocardial infarction (MI) are 25% and 38% in men and women, respectively (7). In our country, clinical signs of CHD are revealed in every 8th woman aged from 45 to 54 years, and in women older than 65 years CHD signs are revealed already in 30%; in Russia, approximately 300,000 women die annually from CHD (1, 8).

Early reports on the coronary angioplasty outcomes demonstrated that the rate of successful intervention was lower in women compared to men (5). It has been suggested that the reasons of this might be lesser vessel diameter in women even taking into account body surface area as well as commonly observed diffuse lesion of coronary vessels, which is less favorable for the surgical treatment (9). Wide introduction of stents and new antithrombotic drugs in the clinical practice significantly improved PCI outcomes (3, 10).

Objective of the study. To investigate the efficacy of invasive treatment in women with CHD.

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Material and methods

Within the period from January 2006 to December 2010, 2790 women with CHD were treated in A.A. Vishnevsky 3rd Central Military Clinical Hospital, percutaneous coronary intervention (PCI) was performed in 284 (10.2%) patients.

Clinical features of CHD were determined using terminology and diagnostic criteria developed and approved by the Scientific Council of the All-Soviet Union Cardiology Scientific Center of the Academy of Medical Sciences of the USSR (1984) based on the proposals of the WHO Expert Committee (12); functional class (FC) of stable angina (SA) – according to the Canadian Cardiovascular Society (4); FC of unstable angina (UA) – according to Hamm C.W. and Braunwald E.A (6); stage/FC of chronic hearth failure (CHF) – according to CHF classification approved by the National Society of Heart Failure Specialists, 2002 (2).

PCI was recommended in: 196 women with stable angina (SA) of FC III-IV, 66 women with unstable angina (UA) and 22 women with myocardial infarction (MI); mean age of patients with SA and UA was 69.5 ± 0.5 years, and mean age of patients after MI was 68.7 ± 1.1 years.

32.8% of women with stable angina had history of MI with formation of postinfarction cardiosclerosis. The concomitant diseases included arterial hypertension (AH) (88.6%), obesity (14.3%), diabetes mellitus (DM) (12.6%), and chronic renal failure (4.5%). Atrial fibrillation (prior to or at the time of admission) was diagnosed in 25.7% of patients with SA. Clinical signs of chronic heart failure stage I (FC I) were observed in 8.6% of women, stage IIA (FC II) in 40% of women, stage IIB (FC III) in 31.4% of women, stage III (FC IV) in 2.8% women. Ischemic ECG changes at rest were observed in 78.7% of women. EchoCG revealed hypokinesis or akinesis/dyskinesis of the cardiac walls in 42.6% cases; left ventricle ejection fraction (LVEF) was 53 ± 0.6%. 44% and 56% SA patients underwent stress test (cycle ergometry or treadmill test) and 24-hour (Holter) monitoring, respectively; myocardial ischemia was confirmed in 33.9% and 47.7% of patients, respectively. Coronary angiography (CAG) revealed hemodynamically significant one-vessel coronary artery disease in 36.9% of patients, two-vessel coronary artery disease in 32.2% of patients; three-vessel coronary artery disease - in 30.9% of patients. The LAD was involved in 41.1% cases, the CxA - in 30% cases, and the RCA - in 27.3% of cases.

Unstable angina manifesting as new-onset angina was diagnosed in 9.8% of women, as progressive exertional angina – in 82.4% of women, early postinfarction angina – in 7.8% of women; patients with primary UA developed without extracardiac factors FC IB and IIB were predominant. LVEF measured by EchoCG was $53.8 \pm 0.3\%$. CAG revealed hemodynamically significant one-vessel disease in 40.8% of cases, two-vessel disease – in 30.6% of cases and three-vessel disease – in 28.6% of cases; the LAD was involved in 42.7% of women, the CxA in 25% of women, and the RCA – in 30.1% of cases.

Non-ST elevation myocardial infarction (NSTEMI) was diagnosed in 12 women; ST elevation myocardial infarction (STEMI) in 10 women. 16 and 6 patients had primary and recurrent MI, respectively. The incidences of concomitant diseases were as follows: arterial hypertension - in 81.8% of patients, postinfarction cardiosclerosis - in 28.1%, diabetes mellitus - in 15.4%, obesity - in 14.7%, chronic renal failure - in 2.9%. Atrial fibrillation (prior to or at the time of admission) was diagnosed in 18.7% of patients with MI. These patients had systemic hemostasis abnormalities characterized by significant (relative to normal values) decrease of hematocrit, platelet count, activated partial thromboplastin time and increased fibrinogen level. The significant changes were revealed in lipid panel, and there were no significant changes in carbohydrate and nitrogen metabolism. Abnormalities on resting ECG (automatism, excitability, and conduction disturbances) were observed in 87.5% of cases; scars and ischemic changes were observed in 22.7% and 65.1% of cases, respectively. Average LVEF measured by EchoCG was $48.9 \pm 0.8\%$, and 28% women who admitted for treatment had LVEF <40%. CAG revealed hemodynamically significant one-vessel disease in 22.7% of cases, two-vessel disease – in 31.9% of cases and three-vessel disease – in 45.4% of cases; the LAD was involved in 38.4% of women, the CxA – in 25.7% of women, and the RCA – in 35.9% of cases.

In case of occluded symptom-related or infarct-related CA, mechanical recanalization using guidewire followed by predilatation of the occluded part of the vessel and stenting of the residual stenosis was performed. In case of subtotal stenosis of symptom-related or infarctrelated CA, the predilatation of the occluded part of the vessel and stenting of the residual stenosis were performed. In case of stenosis of symptom-related or infarct-related CA >70%, the direct stenting was performed. Bare metal stents were implanted in 69% of patients; drugeluting stents were used in 31% of patients. Adjunctive antithrombotic therapy for SA included clopidogrel 300 mg and acetylsalicylic acid 300 mg p/o within 6 hours prior to the coronary angioplasty; in ACS - clopidogrel 600 mg and acetylsalicylic acid 300 mg p/o before transfer to the interventional radiology operating room. In the beginning of the intervention on the coronary arteries, non-fractionated heparin was administered as intra-arterial bolus at a dose of 70-100 IU/kg followed by additional heparin doses under control of activated clotting time at the level of 250-300 seconds. The antithrombotic therapy in 5 MI women was supplemented with Monofram, platelet IIb/IIIa receptor inhibitor (ZAO Framon, Russia). The drug was administered intravenously as a bolus 10-30 minutes prior to the intervention on the CA for 3-5 minutes at a dose of 0.25 mg/kg body weight. After the intervention, patients with ACS received subcutaneously the low-molecular-weight heparin at a medium average therapeutic dose for 24 hours. Introducer sheath was removed from the femoral artery not later than 6 hours after PCI (ACT < 175 sec). After all interventions, regardless of CHD type, aspirin 100 mg/day p/o and clopidogrel 75 mg/day p/o were recommended to be continued for 12 months.

Results and discussion

All women who underwent PCI had coronary flow TIMI III; the residual stenosis in the coronary arteries did not exceed 20%. The average number of implanted stents per one patient was 1.2. Patients with SA had 2 (1%) complications: CA perforation requiring urgent coronary artery





Figure 1. Female patient A., 80 years old. Diagnosis: CHD; transmural myocardial infarction of the posterior wall of the left ventricle: $\mathbf{a} - \text{ECG}$ at the time of admission to the Hospital (3 hours after MI onset); $\mathbf{b} - \text{ECG}$ after primary coronary angioplasty followed by RCA stenting; $\mathbf{c} - \text{ECG}$ recorded 12 hours after endovascular intervention.

bypass grafting. There were no lethal outcomes. In-hospital mortality in women with SA receiving conservative therapy was 0.9%.

There were no complications and lethal outcomes in patients with UA after coronary angioplasty with stenting. In-hospital mortality in patients with UA receiving conservative therapy was 0.7%.

During PCI, one patient with MI (4.5%) had bleeding from the access artery (femoral artery) resulting in the formation of large subcutaneous hematoma which did not affect the outcome; one patient (4.5%) died. The death was caused by acute left ventricular failure not responding to intra-aortic balloon pump and intensive pharmacological therapy. In-hospital mortality in patients with MI who got conservative therapy was 19.5%.

Clinical case of successful coronary angioplasty with stenting in STEMI patient

Female patient, aged 80 years, was admitted to the Hospital by ambulance 3 hours after the onset of angina attack. At the time of admission: blood chemistry – CPK and CPK-MB levels > 5 UNL, hypercholesterolemia, hypertriglyceridemia, leukocytosis; ECG: peracute phase of transmural MI of LV inferior wall (fig. 1 a), EchoCG – hypokinesis of the posterior and apical segment of the hypertrophied left ventricle.

Aspirin 300 mg and clopidogrel 600 mg were given orally. The patient was transferred to the cath-



Figure 2. Female patient A., 80 years old. Diagnosis: CHD; transmural myocardial infarction of the posterior wall of the left ventricle: \mathbf{a} – initial CAG – ~50% tandem stenosis of the middle segment of LAD (arrow), there is no opacification of the distal segment of the RCA from the LCA; \mathbf{b} – occlusion of the middle segment of the RCA (arrow); \mathbf{c} – angioplasty and stenting of the RCA (balloon is marked by the arrow); \mathbf{d} – restoration of RCA lumen (implanted stent is marked with arrow).

lab 75 minutes after admission to the hospital. CAG: the left main coronary artery (LCA) – irregular contours, the left anterior descending artery (LAD) – irregular contours of the proximal segment, ~50% stenosis of the middle segment, the circumflex artery (CxA) – irregular contours at the ostium, the right coronary artery (RCA) – occlusion of the proximal segment, the distal segment cannot be visualized (fig. 2, a, b). Mechanical recanalization of the RCA occlusion was performed using a guidewire (fig. 2 c). Antegrade blood flow through RCA was restored; Cypher stent (Johnson & Johnson, USA) 3.5 mm x 28 mm was implanted into the proximal segment of the RCA. Control CAG after the intervention revealed adequate stent localization, patent arterial lumen, no angiographic signs of intimal dissection, satisfactory hemodynamics in the dilated segment and filling of distal portion of the artery (fig. 2 d).

Accelerated ECG-changes over time were observed (fig. 1b, 1c), polytopic ventricular extrasystoles (as a manifestation of the reperfusion syndrome). Paroxysmal atrial fibrillation developed after the intervention was stopped with parenteral cordarone 300 mg. The further course of the disease was uncomplicated; on Day 14 the patient was discharged to the rehabilitation center in fair condition.

Conclusions

The efficacy of invasive treatment of CHD in women (especially in those at high risk of cardiac complications) is noninferior to that in men. The Mi-related mortality rate in women who underwent angioplasty and stenting of the coronary arteries was 4.3 times lower than in women who received conservative therapy (4.5% versus 19.5%).

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Results of Endovascular Treatment of Patients with Non-QWave Myocardial Infarction

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The article is devoted to endovascular treatment of patients with non-Q wave acute myocardial infarction in the municipal clinical hospital No.15 named after O.M. Filatov. The coronary artery lesions detected during the coronary angiography have been reviewed in the article, the technique of endovascular treatment has been offered, endovascular treatment has been conducted and the results have been assessed.

Results of coronary angiography conducted in 456 patients (241 males and 215 females) with non-Q wave acute myocardial infarction aged from 32 to 76 years have been analyzed. The mean age of patients was 58.4 ± 2.2 years. When conducting the endovascular procedures, transluminal angioplasty and/or stenting of the coronary arteries, balloon catheters and both drug-coated and uncoated stents have been used.

Key words: coronary heart disease, non-Q wave myocardial infarction, coronary arteries, coronary angiography, transluminal angioplasty of the coronary arteries, coronary artery stenosis.

In the Russian Federation, the total incidence of CHD was 4890.1 per 100,000 people and incidence of acute myocardial infarction (AMI) was 144.3 per 100,000 people. The incidence of unstable angina and non-Q wave myocardial infarction was 54.3 per 100,000 people (5). Until recently, non-ST elevation myocardial infarction has been diagnosed mainly based on ECG criteria and clinical symptoms; only a small amount of patients underwent enzyme studies. Overall, the uniform conclusion has been made: a smaller volume of necrosis and lower mortality rate are typical for non-ST elevation myocardial infarction during in-hospital treatment as compared with ST-elevation myocardial infarction. However, during the long-term follow-up, the mortality rate in patients with non-ST elevation myocardial infarction appeared to be higher than in patients with ST-elevation myocardial infarction. An increased risk of early post-infarction angina, recurrent myocardial infarction and sudden coronary death was also observed in patients with non-ST segment elevation myocardial infarction (7, 9, 19).

Recently, the problem of non-ST elevation myocardial infarction has drawn the attention of a large number of studies (11, 12, 13, 14, 21). This can be explained by the fact that percentage of non-ST elevation myocardial infarction is

increasing in the overall number of patients with myocardial infarction. According to R. Goldberg data (23), the number of such patients has increased by 93% from 1975 till 1985, and the number of *ST*-elevation myocardial infarction (MI) has increased by 24% during the similar time period. A wide use of thrombolytic therapy and implementation of angiographic procedures into the clinical practice have caused such changes.

A problem of diagnostics, pathogenesis and treatment of nontransmural myocardial infarction (non-*ST* elevation MI) remains one of the most important problems in the modern cardiology (6, 15, 16).

Tactics and strategy of non-*ST* elevation myocardial infarction treatment has significantly changed which was caused by the changes in the overall state of clinical medicine (11, 14, 20, 21). The last decades were marked by significant success: different groups of beta-adrenoblockers, calcium antagonists have been used; statins with their action aimed not only at decreasing cholesterol level, but also at stabilizing atherosclerotic plaques, have appeared and have been implemented, as well as cytoprotective agents and many other next-generation drugs. Undoubtedly, evolution of therapy

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¹ Non-Q wave myocardial infarction (non-ST elevation myocardial infarction) is an acute process of myocardial ischemia that is rather severe and lasts long enough to cause myocardial necrosis. There are no ST elevations on the baseline ECG(s). Most of the patients with manifesting non-ST elevation myocardial infarction do not develop Q waves on the ECG, and eventually they are diagnosed with non-Q wave myocardial infarction. Non-Q wave myocardial infarction differs from unstable angina by elevated levels of myocardial necrosis markers which are absent during unstable angina (Oganov R.G., Fomina I.G. "Heart Diseases", 2006, pp. 414–415).

Results of Endovascular Treatment of Patients with Non-Q Wave Myocardial Infarction

has made its impact on prognosis, course and treatment of myocardial infarction. Treatment has to be improved by finding a balance between the medical therapy and surgical tactics as a more rational approach for such category of patients (3, 7, 18).

Patients with non-Q wave myocardial infarction remain one of the most complex categories of patients for the invasive treatment; thus, one should systematize the accumulated experience and develop algorithms for management of such patients. The history of non-Q wave myocardial infarction, on the one hand, generally indicates atherosclerotic lesions of the coronary arteries; and on the other hand, the presence of preserved myocardium requires to determine an optimal tactic for preventing repeated infarctions and for improving the long-term prognosis. The absence of Q wave on the electrocardiogram after the acute coronary syndrome suggests that there are no transmural changes in myocardium (1, 3, 4, 5, 10, 18). Nevertheless, the long-term prognosis in patients with a history of non-Q wave myocardial infarction remains unsatisfactory and is associated with the increased risk of repeated coronary complications (3, 4). In patients with achieved reperfusion, there still are morphologic lesion substrate (stenotic atherosclerotic plaque) and viable myocardium in the vascular basin of the infarct-related artery.

Materials and methods

A total of 456 patients (241 males; 215 females) aged from 32 to 76 with non-Q wave acute myocardial infarction have been enrolled in the study. The mean age of patients was 58.4 ± 2.2 years.

Myocardial infarction has been diagnosed based on the presence of two out of three following sings: typical clinical manifestation of pain under the breastbone, changes on serial ECGs and increased level of cardiac enzymes (creatine phosphokinase and its isoenzymes, troponin T) in the plasma with their subsequent decrease.

Clinical and biochemical blood parameters (creatine phosphokinase and its isoenzymes, troponin T) and ECG changes were assessed on admission. All patients underwent coronary angiography within a period from 2 to 30 days after hospitalization. If the pain syndrome recurred, coronary angiography was conducted within 24 hours. All patients received standard therapy: antiaggregants, anticoagulants, beta-blockers, Ca antagonists, ACE inhibitors, nitrates, clopidogrel.

Endovascular treatment of patients included one, two or three stages. The main indications for emergency endovascular treatment of patients with non-*Q* wave MI were as follows: drug resistance (relapsing pain syndrome), worsening based on ECG data, decreased global and regional contractility according to Echo-CG data, abrupt narrowing of a symptom-related artery according to the coronary angiography data.

Indications for the second-stage revascularization in patients with non-*Q* wave MI were as follows: proximal lesion of the left anterior descending artery (LAD) during intervention on other coronary arteries at the first stage; in case of non-symptom-related coronary artery lesions, a positive stress test or "silent" depression of *ST* segment greater than 1 mm; in case of multifocal lesions and severe scarry changes on the ECG making impossible to reliably assess the degree of ischemia; persisting angina attacks after the endovascular intervention (EI) on a symptom-related artery.

Results and discussion

Results obtained during the coronary angiography suggest that the lesion rates in the various coronary arteries of examined patients are similar to total CHD: vascular accidents, in a majority of cases, occurred in the left anterior descending artery (56.4%) and in the right coronary artery (17.5%). The circumflex artery was affected in 9.2% of cases and the left main coronary artery – in 6.8% of cases. Lesions of the second-order branches were relatively rare: in 7.4% of cases for the obtuse marginal branch, and in 2.7% of cases for the diagonal branch.

It should be noted that during assessment of the blood flow in the infarct-related artery, TIMI III was registered in 375 patients (82.2%), TIMI II – in 19 patients (4.2%), TIMI I – in 21 (4.6%) and TIMI 0 – in 41 (9%) patients. The signs of the infarct-related artery spasm were observed in 67 (14.7%) patients (it was managed by intracoronary nitroglycerin).

More than 80% stenosis of the infarct-related artery was detected in 422 (92.5%) patients, occlusion of the infarct-related artery was observed in 18 (3.9%) patients.

Out of 456 examined patients who had hemodynamically significant lesions of the coronary arteries, collaterals (through which distal parts of the occluded or stenotic coronary arteries were retrogradely filled) were found in 84 (18.4%) patients during angiography.

Lesions of the coronary arteries detected after the coronary angiography were quantified as follows: 196 (43%) patients had one-vessel lesion; 123 (27%) patients had two coronary arteries affected, and 137 patients (30%) – more than two coronary arteries affected.

The average values of Troponin T in the groups of studied patients with non-*ST* elevation myocardial infarction (Figure 1).

No significant differences in Troponin T levels were revealed in the groups of studied patients.

Endovascular interventions included the following number of stages: endovascular treatment included one stage in 319 (70%) patients, two stages in 121 (26.5%) patients and three stages in 16 (3.5%) patients.

The results of conducted treatment were as follows: angina attacks completely disappeared and also a high exercise tolerance was observed in 402 (88%) patients; quality of life improved in 380 (83%) patients.

The first group of patients (one-stage endovascular treatment): repeated endovascular procedures were not conducted in 6 patients during hospitalization period (angina has recurred). At the end of 6–12 month followup, 3 repeated MI were registered; 8 patients were repeatedly hospitalized with diagnoses "unstable angina and exertional angina", which required elective coronary angiography (CAG) and endovascular treatment (Table 1).

The second group of patients (two-stage endovascular treatment): at the end of 6–12 month follow-up, 2 repeated MIs were registered, 1 patient died, and 9 patients were repeatedly hospitalized with diagnoses of unstable angina and exertional angina.

Five patients underwent repeated endovascular procedures. Two patients underwent CABG (Table 1).

The third group of patients (multi-vessel lesions in the coronary circulation with both

0.45 0,40 0.35 0.30 0.25 0.20 0.15 0.10 0.05 0.00 Group 1 Group 2 Group 3 (n = 227) (n = 86) (n = 9)

Figure 1.

two- and three-stage endovascular treatment): 1 patient died. Repeated MI was registered in 1 patient. CABG was performed in two patients. Three patients were repeatedly hospitalized (Table 1).

It does not seem possible to compare the groups of patients, as the lesions of the coronary vessels varied in different groups of patients, as well as both drug-coated and uncoated stents were used.

Conclusions

1. Maximally complete revascularization in patients with non-Q wave acute myocardial infarction makes it possible to fully get rid of angina in more than 85% of patients.

2. Endovascular revascularization in patients with non-Q wave infarction decreases mortality down to 0.9%.

3. Subtotal stenosis of the infarct-related artery is the main cause of myocardial damage in 92.5% of patients with non-*Q* wave myocardial infarction.

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| Table 1 | . Results of clinical | observations in | patients during | 6-12 | 2 months of the | post-infarction | period |
|---------|-----------------------|-----------------|-----------------|------|-----------------|-----------------|--------|
|---------|-----------------------|-----------------|-----------------|------|-----------------|-----------------|--------|

| Variable | Group 1 (n = 274) | | Group 2 (n = 109) | | Group 3 (n = 14) | |
|---------------------------------------|----------------------|-----|----------------------|-----|---------------------|------|
| | Abs. | % | Abs. | % | Abs. | % |
| Exertional angina | 2 | 0.7 | 4 | 3.7 | 3 | 21.4 |
| Hospitalization with unstable angina | 6 | 2.2 | 5 | 4.6 | 0 | 0 |
| MI relapses | 3 | 1.1 | 2 | 1.8 | 1 | 7.1 |
| Mortality after hospitalization | - | 0.0 | 1 | 0.9 | 1 | 7.1 |
| Repeated endovascular procedures | 7 | 2.6 | 5 | 4.6 | 1 | 7.1 |
| Coronary artery bypass surgery (CABG) | 0 | 0 | 2 | 1.8 | 2 | 14.3 |

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Endovascular Correction of an Acquired Left Ventricular to Right Atrial Communication Following Surgical Correction of Transposition of the Great Arteries in a Child (A Clinical Case)

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We report the diagnosis and successful endovascular closure of acquired left ventricular to right atrial communication using the Seer Care muscular ventricular septal defect occluder in a 7-year old child after previous radical correction of transposition of the great arteries.

Key words: left ventricular to right atrial communication, transposition of the great arteries, Seer Care occluder.

List of abbreviations:

- iEDV Indexed end-diastolic volume
- ACG Angiocardiography
 - Ao Aorta
- CHD Congenital heart defect
- VSD Ventricular septal defect
 - LV Left ventricle
- LV-RAC Left ventricular to right atrial communication
 - RV– Right ventricle
 - RA Right atrium
 - TV Tricuspid valve
 - TGA Transposition of the great arteries
 - AF Annulus fibrosis

Acquired left ventricular to right atrial communication (LV-RAC) occurs rarely, and due to its great hemodynamic significance is dangerous for a patient. Occurrence of this unusual ventricular septum defect is attributed to infectious endocarditis (2), injury (3), myocardial infarction (4) or complications of intracardiac interventions, e.g. valve replacement or ventricular septal defect (VSD) plasty (1, 7, 8). The diagnosis of this rare complication may be a challenge; however, it was effectively diagnosed using echocardiography or magnetic resonance imaging in some previously reported cases (7, 14). The anatomical types of LV-RAC

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Department of Cardiac Surgery and Intensive care N.F. Filatov City Pediatric Clinical Hospital №13 Sadovaya-Kudrinskaya, 15, Moscow, 123001, Russia E-mail: vnilyin@mail.ru Manuscript received on June 4. 2012. Accepted for publication on August 9, 2012. are shown in Figure 1. The main method of choice for correction of acquired LV-RAC is an open heart surgery; however, successful endovascular closure using occluder device was reported in 7 published cases (1, 7–11). There are only single reports in literature on occurrence of this complication following correction of congenital heart defects (CHD) in children (10), moreover, none after correction of transposition of the great arteries (TGA). We found no reports on endovascular closure of such defect in children less than 8 years old.

Material and methods

In October 2010, a child aged 7 years and 4 months and weighting 21 kg was admitted to the Department of Cardiovascular Surgery and Intensive Care of N.F. Filatov Children's City Clinical Hospital No.13. CHD was diagnosed in the child within the first months of life, and during examination performed at another institution in February 2004, including heart catheterization and angiocardiography (ACG), the following diagnosis was made: situs solitus, D transposition of the great arteries, ventricular septal defect, patent foramen ovale, moderate combined pulmonary artery stenosis, moderate arterial hypoxemia. The surgery was delayed due to relatively good condition of the child. Following the repeat examination in October of the same year (the child's age at that time was 1 year and 4 months) and taking into account increasing arterial hypoxemia, a decision to perform palliative surgery - rightsided modified subclavian-pulmonary anastomosis using Gore-Tex vascular graft (5 mm in diametr) was performed. After the operation,

Endovascular Correction of an Acquired Left Ventricular to Right Atrial Communication Following Surgical Correction of Transposition of the Great Arteries in a Child (A Clinical Case)

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Figure 1. Anatomical types of LV-RAC. The arrow shows tlocalization of left ventricular – right atrial shunt: above the TV (type I), under the TV (type II) and simultaneously in both areas (type III).

arterial blood saturation increased up to 82%, and the child was discharged home in fair condition.

One year later, in October 2005, at the age of 2 years and 5 months, the patient underwent hearth defect correction using cardiopulmonary bypass and hypothermia: arterial switch operation, VSD plasty, pulmonary valvuloplasty, resection of pulmonary subvalvular stenosis, ligation and transection of Gore-Tex vascular graft (subclavian-pulmonary anastomosis). Duration of extracorporeal circulation was 205 minutes. Under Custodiol cardioplegia, the aorta was cross-clamped for 124 minutes. The postoperative period was unremarkable. The child was extubated 72 hours after the surgery. The antibiotic therapy lasted for 12 days. The patient was discharged home in fair condition 13 days after surgery. Echocardiography at discharge: peak systolic gradient on the neoaortic valve (neo Ao) 45 mmHg, no regurgitation; left ventricle ejection fraction - 71%; trivial mitral and tricuspid insufficiency; systolic gradient on the neopulmonary valve - 10 mmHa.

During out-patient examination 8 months after the operation, a coarse systolic murmur was heard over the heart area, and X-ray showed increased heart dimensions. A followup transthoracic EchoCG reveled a LV-to-RA shunt through septal defect measuring 5 mm and located 3-4 mm below the neoaortic valve, mistakenly considered as residual VSD with TV regurgitation. The following therapy for congestive heart failure was prescribed: digoxin, verospiron, limitation of physical exertion and systematic follow-up. At the next scheduled examination in July 2008 (2 years and 9 months after the operation), the diagnosis was clarified using echocardiography: LV-RAC.

On October 01, 2010, the child was admitted to the Department of Cardiovascular Surgery of N.F. Filatov Children's City Clinical Hospital No.13 for defect correction. Physical examination: moderately severe condition; complaints of frequent respiratory infections; the skin is pale pink, fair nutritional status, no edema; no dyspnea at rest, moderate dyspnea on exertion; breathing is symmetrical, there are no rales; heart sounds are rhythmical, HR 68 bpm, coarse systolic murmur over the heart area, peripheral artery pulse is symmetrical with adeguate guality, BP 110/62 mmHg without gradient between upper/lower extremities; the liver extends 1.5 cm below the costal margin; the child receives no specific drug therapy. Electrocardiography: sinus rhythm at a rate of 68 beats per minute, normal position of the electrical axis of the heart, left posterior fascicular block. Echocardiography: indexed LV enddiastolic volume (iEDV) - 120 ml/m²; LV ejection fraction - 70%; mitral annulus fibrosis (AF) Z score \emptyset +0.95, no regurgitation; neo-Ao valve has 2 cusps, cusps are indurated, AF Z score Ø +3.17, LV/Ao peak systolic gradient – 42 mmHg, no regurgitation; ascending Ao Z-score +2.89; RV iEDV – 83 mL/m²; RA – 40 x 34 mm; tricuspid AF Z-score Ø +2.05, trivial regurgitation; color Doppler mapping of the ventricular septum shows a patch fixed to VSD without residual shunt; ostium measured up to 6 mm is observed in the atrioventricular part of the membranous septum which connects the left ventricle to right atrium (LV-RAC, type I), with systolic gradient 103 mmHg; interatrial septum is intact.

Given technical difficulties and the risk of repeated surgery under cardiopulmonary bypass, it was decided to perform angiocardiography and then – to attempt endovascular closure of LV-RAC.

Surgical technique

Left ventriculography in four chamber view revealed the shunt of contrasted blood through the communication between LV and RA, its diameter at the site of maximal narrowing was 4 mm (Figure 2). The aortic arch was right-sided. The isthmus was not narrowed. Neo-Ao cusps were asymmetric, thickened; systolic gradient measured by direct manometry was 45 mmHg. Neo-Ao obturative function was adequate. It was revealed, that the edges of defect were located far enough away from the neo-Ao valve on the side of LV (4 mm) and from the tricuspid valve on the side of RA (3 mm). The decision was made to close LV-RAC using the Seer Care muscular VDS occluder.

Right coronary catheter was introduced through the femoral artery, aorta, LV, and LV-RAC to the right atrial cavity. A long guidewire (260 cm) was placed into RA through the catheter. A snare of 25 mm in diametr was introduced through the femoral vein, inferior vena cava to the RA cavity; the guidewire was introduced into the femoral vein using this snare; arterial-venous loop was formed. The Seer Care delivery system 5 Fr was placed using venous access in the LV cavity though the guidewire. The guidewire was removed. An attempt to close LV-RAC using the Seer Care occluder 4 mm was performed; however, optimal position of the device was not achieved. The occluder was removed. The arterialvenous loop was formed again. The Seer Care delivery system 6 Fr was placed using arterial access in the RA cavity through the guidewire. LV-RAC was successfully closed using the Seer Care occluder 6 mm (Figure 3). After detaching the occluder from its delivery system, a followup left ventriculography was performed; no abnormal shunt was observed in the right atrium (Figure 4). Occluder placement was guided by transthoracic echocardiography; this examination confirmed complete termination of blood flow through LV-RAC.

Results

No surgical complications related to this endovascular intervention were reported. The child was transferred from the interventional radiology operating room to the surgical ward. Sinus bradycardia (50 bpm) was observed in the first 24 hours of post-operative period. No specific drug therapy for the heart rhythm acceleration was prescribed, because the child had no other hemodynamic disorders and neurological deficiency. 24-hour ECG monitoring



Figure 2. Left ventriculgography. The asterix marks the communication between the LV and the RA. One can see opacified blood shunting from the LV to the RA cavity.

excluded prolonged pauses in the heart rhythm which could induce syncopal conditions, and demonstrated return to sinus rhythm which is usual for the child (68–74 bpm) within two days. The duration of hospitalization was 8 days. No treatment for congestive heart failure was required. Aspirin 3 mg/kg/day was prescribed.

Ten months later, the child had control echocardiography: LV iEDV - 82 ml/m²; LV ejection fraction – 72%; mitral AF Z-score \emptyset +1.89, no regurgitation; neo-Ao valve has 2 cusps, the cusps are indurated, their mobility is limited, AF Z-score Ø +4.58, cusps opening Z-score Ø -3.64; peak systolic gradient LV/Ao 45 mmHg, no regurgitation; ascending Ao Z-score +4.86; RV iEDV 61 mL/m²; RA 34 × 36 mm; tricuspid AF Z-score \emptyset +2.55, minimal regurgitation; the echocardiographic signal from the occluder is observed in the atrioventricular part of the membranous septum (Figure 5). No blood shunt was observed, ventricular septum movement is normal; interatrial septum is intact; pericardial cavity contains no liquid.

Discussion

Acquired LV-RAC is observed rarely, although there is an opinion that the incidence of clinical observations increases within the last 10-20 years due to increased number of patients who underwent cardiovascular intervention (11). The diagnosis of this complication may be a challenge. The optimal conditions for LV-RAC identifying are provided by transthoracic echocardiography using parasternal and

Endovascular Correction of an Acquired Left Ventricular to Right Atrial Communication Following Surgical Correction of Transposition of the Great Arteries in a Child (A Clinical Case)



Figure 3. Seer Care occluder (6 mm in diameter) is inserted in the LV-RA communication via transarterial approach. The asterix marks the occluder's position.



Figure 4. Control left ventriculography. The shunt of opacified blood from the LV to the RA is absent. The asterix marks the occluder's position..



Figure 5. Transthoracic EchoCG, four-chamber view. The asterix marks the echo signal from the occluder

apical position so called four-chamber projections. Sometimes it is difficult to distinguish the blood flow through VSD and tricuspid regurgitation from LV-RAC. Observed high-velocity blood flow in this area may be interpreted as an evidence for tricuspid regurgitation due to high pulmonary hypertension (13). Nevertheless, the diagnostic mistake may be avoided if the possibility of LV-RAC is considered, and comprehensive analysis of shunt direction and assessment of diastolic pressure in PA based on valve regurgitation is performed. Transesophageal echocardiography may significantly improve the precision of diagnosis of nature of this shunt (14). Magnetic resonance imaging provides the good possibility for the diagnosis of this heart defect.

While analyzing the known reasons for LV-RAC listed at the beginning of our report, we have taken note of the concept focusing at the results of surgical manipulations intended to remove the calcium during aortic and mitral valve replacement, as a reason for thinning and weakening of membranous septum leading to the defect formation. In this case, during arterial switch operation we had to correct moderate stenosis of LV outflow tract by resection of fibrous and muscular cushion under the PA valve. Obviously, these manipulations resulted in insignificant lesion of membranous septum, which led to the formation of a large LV-RAC in the long-term postoperative period.

The primary congenital and acquired LV-RACs are usually closed surgically under cardiopulmonary bypass. However, repeated operations are known to be associated with the additional risk of serious complications; therefore, endovascular method of LV-RAC closure using occuders after previous operations seems to be preferable. There are reports on 7 successful clinical observations in literature (1, 7–11). Six adult patients previously underwent mitral valve replacement and one patient – VSD closure.

It is known that anatomically tricuspid valve is located several millimeters (from 4 mm in children and up to 15 mm in adults) below the mitral valve (12). Therefore, LV-RAC may be located in this space above the TV (type I), below the TV (type II) and in both areas simultaneously (type III) (Figure 1). The patients had type I LV-RAC in all previously reported observations of endovascular occlusion, as well as in our case. The attempts to apply this method for other types of LV-RAC may theoretically affect the function of the tricuspid valve.

In four published reports, acquired LV-RAC were closed using Amplatzer duct occluders, in one case - by VSD occluder, and in two cases - by IASD occluders. No published cases reported serious complications and significant residual shunts. We successfully and completely closed the defect using the Seer Care occluder developed for occlusion of muscular VSD. It is important to emphasize that placement of this occluder was not associated with the impairment of tricuspid and neoaortic valve function, and the achieved RLV-RAC occlusion is sustained for 10 months after the intervention.

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The Association Between Chronic Ischemic Mitral Regurgitation and the Localization of Coronary Stenoses in Patients with Postinfarction Cardiosclerosis

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The comparison of 626 patients with postinfarction cardiosclerosis without mitral regurgitation versus 139 patients with moderate-to-severe mitral regurgitation revealed that chronic moderate-to-severe mitral regurgitation is associated with the right coronary artery stenosis in middle-aged men with postinfarction cardiosclerosis. Our data indicate the importance of timely restoration of blood flow in the right coronary artery during myocardial revascularization in this setting.

Key words: mitral regurgitation; coronary stenoses; postinfarction cardiosclerosis.

List of abbreviations

- CHD coronary heart disease
 - MI myocardial infarction
 - LV left ventricle
- MR mitral regurgitation
- RCA right coronary artery

Objectives. To determine whether MR is associated with the localization of coronary stenoses in CHD patients with postinfarction cardiosclerosis.

Background. The results of studies investigating the relationship between ischemic mitral regurgitation (MR) and localization of postinfarction cardiosclerosis are controversial, while the studies investigating the association with topical coronary lesions are few in number.

Methods. Middle-aged men with postinfarction cardiosclerosis were selected: 626 patients without MR and 139 patients with moderate-to-severe MR.

Results. Patients with MR had higher incidence of more severe classes (III–IV) of heart failure by NYHA (33.3 versus 10.9%, p < 0.001), arterial hypertension grade III (34.3 versus 22.1%, p = 0.003), and repeated myocardial infarction in history (15.8 versus 9.7%, p = 0.031);

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however, they had lower total cholesterol levels $(5.1 \pm 1.3 \text{ versus } 5.5 \pm 1.2 \text{ mmol/L}, \text{ p} = 0.001).$ Echocardiographic parameters in this patients were as follows: larger asynergy of the left ventricle (LV) (34.7 ± 15.4 versus 24.4 ± 12.8%, p < 0.001), larger linear dimensions of the heart cavities including left atrium (23.2 \pm 2.6 versus $20.4 \pm 1.8 \text{ mm/m}^2$, p < 0.001) (with exception of tendency for lesser LV posterior wall thickness in MR patients - 5.3 ± 0.6 versus 5.2 ± \pm 0.8 mm/m², p = 0.073). MR patients had more frequently LV dilatation (71.2 versus 21.1%, p < 0.001), reduction of its contractility (73.2 versus 27.2%, p < 0.001); lesion of the right coronary artery (59.0 versus 43.8%, p = 0.001) and stenosis of obtuse marginal branch of the left coronary artery (15.1 versus 6.9%, p = 0.002). The multivariate analysis showed the independent relationship with MR for: stenosis of the right coronary artery, increased left atrium dimensions, and decrease in LVEF, total cholesterol level, and LV posterior wall thickness.

Conclusions. In middle-aged men with postinfarction cardiosclerosis, the chronic moderate-to-severe MR is associated with the right coronary artery stenosis.

Introduction

Disturbances of papillary muscles and chordal system in absence of significant lesion of mitral cups, local myocardial contractility impairment and abnormal left ventricular (LV) remodeling followed by dilatation and enlargement of the mitral fibrous ring (1) play role in the development of mitral regurgitation (MR) in

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coronary heart disease (CHD). Ischemic MR may be caused by rupture of the papillary muscles, dysfunction of isolated group of the papillary muscles (more common) and regional abnormal LV remodeling (in the majority of cases) leading to chordal tension and incomplete closure of mitral cusps due to displacement of the median-posterior papillary muscle to the LV apex or backwards. In CHD patients, MR may be caused by generative changes, especially in elderly patients (2).

The results of studies investigating the relationship between MR and localization of the scary lesions of the myocardium are rather controversial: some authors believe that MR is clearly associated with the localization of the myocardial infarction (MI) (1, 3-5), other authors reported lack of such correlation (6-8)Since depending on the type of coronary blood flow, the same myocardial area may be supplied by different coronary arteries, and the same asynergy area may be associated with the different localizations of hemodynamically significant coronary stenosis. We considered that the search of a probable relationship between the ischemic MR and the localization of coronary lesions is relevant. There are few data in literature about the relationship between MR and the localization of the coronary stenoses and they mainly relate to MR in acute forms of CHD (4, 9-12).

The objective of this study is to determine whether chronic moderate-to-severe MR in patients with postinfarction cardiosclerosis is associated with the localization of the coronary stenoses.

Methods

Men aged from 44 to 55 years with a history of Q-wave MI (626 patients without MR and 139 patients with MR grade 2 and above) were selected and divided in groups from 15,283 patients included in the Coronary Angiography Registry[®] (13) within the period from 1991 to 2012. Patients with MR grade less than 2, acute MI, cardiac defects, unsatisfactory visualization by echocardiography were not enrolled in the study. The patients underwent: clinical and complex echocardiographic examinations (using Imagepoint NX, Agilente Technologies -Phillips – USA; Vivid 3, 4, 7 Systems, Vingmed General Electric – Horten – Norway), serum lipid profile determnation, Holter monitoring, selective CAG by Judkins method (1967) using angiography units Diagnost ARC A, Poly Diagnost C, Integris Allura (Phillips - Holland. The echocardiographic syndromes were diagnosed in accordance with the standard criteria: LV systolic function was considered to be reduced if LV ejection fraction was <50%; LV was considered to be dilated if the end-diastolic dimension was >55 mm; MR was considered to be of grade ≥ 2 if the effective area of regurgitation orifice was ≥0.2 cm², and regurgitation volume ≥30 ml (14). Linear echocardiographic parameters and myocardial mass calculated using Devereux formula (15), were indexed to the body surface area. Statistical processing was performed using statistical software package (SPSS Inc., version 11.5). The values were presented as M ± SD. The distribution of variables was determined using Kolmogorov-Smirnov test. The normally distributed values were compared using Student t-test, and on case of non-normal distribution - non parametric Mann-Whitney test was used. The qualitative parameters were analyzed using Pearson χ^2 test. p<0.05 was considered to be statistically significant. The multivariate analysis (binary logistic regression and odds ratio) was performed.

Results

There were no differences in age, body mass index, smoking, CHD hereditary problems, and arterial hypertension between groups. MR patients had significantly higher incidence of more severe functional classes (III–IV) of circulatory failure according to New York Heart Association (NYHA), grade III arterial hypertension and anamnestic myocardial reinfarction (Table 1). There were no between-group differences in years after MI, angina functional classes according to Canadian Cardiovascular Society and the incidence of statin use (95.4 versus 96.5%), total cholesterol levels and incidence of diabetes mellitus were higher in non-MR patient.

In our study, grade 2 MR was observed in 16.7% of patients, grade 3 MR – in 1.4% of patients. The analysis of echocardiography parameters (Table 2) showed that MR patients had significantly higher myocardial mass indices and larger linear dimensions of the heart cavities except for ventricular septum thickness (no differences between groups were observed) and LV posterior wall (MR patients had significantly lesser values). Mean LV ejection fraction in this population was lower than normal compared to that in non-MR patients, they had more frequently heart rhythm disturbances and LV aneurisms including aneurisms

The Association Between Chronic Ischemic Mitral Regurgitation and the Localization of Coronary Stenoses in Patients with Postinfarction Cardiosclerosis

| Parameters | Patients without MR (n = 626) | Patients with MR (n = 139) | р |
|------------------------------------|----------------------------------|-------------------------------|---------|
| Age, years | 49.2±3.0 | 49.7±3.1 | NS |
| Smoking, % | 49.8 | 54.7 | NS |
| CHD hereditary problems, % | 15.8 | 12.6 | NS |
| Body mass index, kg/m ² | 29.3±4.3 | 29.1±4.2 | NS |
| Arterial hypertension, % | 60.7 | 68.3 | NS |
| Arterial hypertension grade, % | | | |
| I–II | 32.5 | 32.9 | NS |
| | 22.1 | 34.3 | 0.003 |
| Diabetes mellitus, % | 8.1 | 5.7 | 0.008 |
| FC NYHA | | | |
| | 89.1 | 66.6 | < 0.001 |
| III–IV | 10.9 | 33.3 | <0.001 |
| Total cholesterol (mmol/L) | 5.5±1.2 | 5.1±1.3 | 0.001 |
| Exertional angina FC | | | |
| I–II | 46.6 | 48.5 | NS |
| III–IV | 53.4 | 51.5 | NS |
| Years after myocardial infarction | 2.5±3.4 | 2.7±3.9 | NS |
| Number of myocardial infarction | | | |
| 1 | 88.7 | 82.0 | 0.030 |
| 2 | 9.7 | 15.8 | 0.031 |
| ≥3 | 1.6 | 2.2 | NS |

Table 1. Comparison of clinical and functional and laboratory parameters in CHD patients with postinfarction cardiosclerosis depending on mitral regurgitation

 $M \pm SD$ – mean \pm standard deviation; MR – mitral regurgitation; FC – functional class; NYHA – New York Heart Association; NS – not significant.

with thrombus. Mean size values and LV asynergy index were higher in MR group. In this group, the incidences of reduced LV systolic function and LV dilatation were 2.7 and 3.4 times higher. There were no differences in the localization of postinfarction cardiosclerosis, incidence of aortic atherosclerotic lesion detection and aortic root diameter between groups. Non-MR patient demonstrated a tendency to more frequent detection of additional diagonal chords in LV.

With regard to angiographic parameters (Table 2), stenoses of the right coronary artery (RCA) and obtuse marginal branch of the left coronary artery were observed more frequently in MR patients, while stenoses of diagonal branch of the left coronary artery were observed more frequently in non-MR patients. A tendency to more frequent detection of two-coronary vessel disease and right-sided coronary blood supply type was observed in MR patients, and the balanced type coronary blood supply was observed more frequently in non-MR patients.

The multivariate analysis (Table 3) demonstrated the independent relationship between MR and RCA stenoses, increased left atrium volume index, decreased LV ejection fraction, decreased total cholesterol level, and decreased LV posterior wall index. The odds ratio calculation revealed 2.1-fold increase in MR risk in the presence of the RCA stenoses; with the increase of the left atrium volume index by each mm/m² – by 87%; with decrease in LV ejection fraction by each 1% – by 7%; with decrease in total cholesterol level by each 1 mmol/L – by 31%, with decrease in LV posterior wall thickness index by each 1 mm/m² – by 49%.

Discussion

Of note, no patients with insignificant MR were enrolled in the study because such regurgitation is considered to be physiological in some cases. Therefore, the main group included only patients with abnormal regurgitation (moderate to severe).

Patients with acute CHD were not enrolled in this study, as in these cases MR is reversible more frequently, especially after successful reperfusion (16). According to Borger M.A. et al. definition (17), chronic ischemic MR occurs at least one week after MI, and is mandatory accompanied by local LV contractility abnormalities and hemodynamically significant coronary stenoses; and MV cusps and chords should not have significant lesions (17). Inclusion criteria for our study comply fully with this definition. Finally, only middle aged men were enrolled in the study to exclude the influence of age and gender.

| Parameters | Patients without MR (n = 626) | Patients with MR (n = 139) | Р | | |
|---|----------------------------------|-------------------------------|-------------|--|--|
| Echocardiographic parameters | | | | | |
| Aortic root diameter | | | | | |
| mm | 34.7±3.1 | 35.0±3.4 | NS | | |
| mm/m ² | 17.7±1.9 | 17.7±2.1 | NS | | |
| Left atrium diameter | | | | | |
| mm | 42.1±5.9 | 47.1±6.2 | < 0.001 | | |
| mm/m² Dialaturantiala dimension | 20.4±1.8 | 23.2±2.0 | <0.001 | | |
| Right ventricle dimension | 24 6+2 2 | 26 9+3 9 | < 0.001 | | |
| mm/m ² | 12.5±1.3 | 13.6±2.2 | <0.001 | | |
| Left ventricle diameter | | | | | |
| mm | 51.8±5.2 | 59.4±7.2 | <0.001 | | |
| mm/m ² | 25.8±2.7 | 29.7±4.0 | <0.001 | | |
| Ventricular septum thickness | | | | | |
| mm | 12.3±2.0 | 11.7±2.3 | 0.004 | | |
| mm/m² | 6.0±1.0 | 5.9±1.2 | NS | | |
| Left ventricle posterior wall thickness | 10 7+1 2 | 10 2+1 6 | 0.001 | | |
| mm/m^2 | 5.3±0.6 | 5.2 ± 0.8 | 0.073 | | |
| Myocardial mass | | 012 010 | 0.070 | | |
| g | 279.7±72.4 | 332.7±93.1 | <0.001 | | |
| g/m ² | 132.0±26.7 | 165.4±45.6 | <0.001 | | |
| LV ejection fraction,% | 52.6±7.2 | 43.3±9.5 | <0.001 | | |
| LV asynergy, % | 24.4±12.8 | 34.7±15.4 | <0.001 | | |
| LV dilatation, % | 21.1 | 71.2 | <0.001 | | |
| Signs of aortic atherosclerotic lesion, % | 90,4 | 87.1 | NS | | |
| Additional chords, % | 11,4 | 5.8 | 0.051 | | |
| Reduced LV contractility, % | 27,2 | 73.2 | <0.001 | | |
| LV aneurism, % | 19,0 | 41.0 | <0.001 | | |
| LV clot masses, % | 5,0 | 11.6 | 0.005 | | |
| Localization of the postinfarction cardiosclerosis, % | 40.7 | 40.5 | NO | | |
| Interior | 42.7 | 40.5 | | | |
| Combined | 26.9 | 26.2 | NS | | |
| | | 2012 | | | |
| Electrocardiographic | | | | | |
| Heart rhythm disturbances, % | 14.8 | 28.6 | 0.001 | | |
| Coronary angiograph | ic parameters | | | | |
| Stenosis of the left main coronary artery*, % | 1.3 | 1.4 | NS | | |
| Stenosis of the left anterior descending artery*, % | 50.5 | 48.2 | NS | | |
| Stenosis of the circumflex artery*, % | 25.6 | 28.8 | NS | | |
| Stenosis of the diagonal branch*, % | 11.0 | 5.0 | 0.033 | | |
| Stenosis of the right coronary artery*, % | 43.8 | 59.0 | 0.001 | | |
| Stenosis of the obtuse marginal branch*, % | 6.9 | 15.1 | 0.002 | | |
| Stenosis of the intermediate branch*, % | 2.2 | 0.7 | NS | | |
| One-coronary vessel lesion*, % | 41.9 | 35.3 | NS | | |
| Two-coronary vessel lesion*, % | 20.6 | 28.1 | 0.054 | | |
| Multivessel lesion*, % | 17.4 | 20.1 | NS | | |
| Type of coronary blood flow, % | 01.4 | 147 | 0.075 | | |
| Left-sided | 13.8 | 14.7 | 0.075 NS | | |
| Right-sided | 64.8 | 72.8 | 0.072 | | |

Table 2. Comparison of echocardiographic, electrocardiographic, and angiographic parameters in CHD patients with postinfarction cardiosclerosis depending on mitral regurgitation

 $M \pm SD$ – mean \pm standard deviation; MR – mitral regurgitation; LV – left ventricle; NS – not significant; * – stenosis of the coronary artery lumen >75%.

| Independent variable | Dependent variable | Odds ratio | 95% CI | Р |
|-------------------------|--|------------|-----------|--------|
| Mitral regurgitation | Stenosis of the right coronary artery* | 2.14 | 1.18-3.87 | 0.012 |
| | Index of the left atrium dimension | 1.87 | 1.57-2.23 | <0.001 |
| | LV ejection fraction | 0.93 | 0.90-0.97 | <0.001 |
| | Total cholesterol | 0.69 | 0.54-0.89 | 0.003 |
| | LV posterior wall thickness | 0.51 | 0.32-0.81 | 0.004 |

Table 3. Parameters independently related to the mitral regurgitation in CHD patients with postinfarction cardiosclerosis

* – stenosis degree of the coronary artery lumen >75%; LV – left ventricle.

Ischemic MR is an independent predictor of cardiovascular mortality with the relative risk of 1.5–7.5 (14). Particularly, MR was proven to increase the risk of cardiovascular mortality in chronic CHD with a history of Q-wave infarction regardless of age and LVEF (18). Both presence of MR and its degree are important: the risk of heart failure increases from 3.4 to 6.8-fold with the increase in MR degree up to moderate or severe within 30 days after MI, the risk of death increases from 1.6 to 2.2-fold (6), and long-term survival decreases 2.3-fold compared to non-MR patients or patients with insignificant MR (19).

According to the European Cardiology Society experts' opinion, chronic ischemic MR occurs due to abnormal tension of subvalvular apparatus in case of LV dilatation and/or dysfunction, especially its posterior and lateral segments (1). According to studies by some authors, the inferior and lateral MI is complicated by ischemic MR more frequently (3–5, 20). However, the anteroapical MI may also cause mechanic displacement of the papillary muscles and development of significant MR even in the absence of LV dilatation (21). The inferior and lateral MI is proven to be associated with less significant dilatation and reduction of global systolic LV function, but are more frequently accompanied by significant MR (3, 4). However, the anterior and anterior-septal MI is less frequently complicated by significant ischemic MR although it causes LV dilatation and dysfunction more frequently (3, 20, 22) Although no between-group differences in the localization of postinfarction cardiosclerosis and depth of previous MI (all Q-wave MI) were observed in our study, the independent relationship between MR and RCA stenoses indicates possible relation between MR and dimensions of scary lesions and adjacent hibernated myocardium which is confirmed by greater dimension of LV asynergy in MR group.

Interestinly, these results are contrary to the data obtained from the previous stage of our

study (23) as well as to the observations of patients with postinfarction cardiosclerosis reported by Nixdorff et al. (8), in which no independent relationship between MR and MI localization, or localization of coronary lesions were determined; MR demonstrated independent relationship between abnormal global LV remodeling, manifested as its dilatation and development of heart failure. This might be due to the fact that our previous report described the database cut-off without any additional selection criteria; therefore, the groups were not comparable by gender and age. The relationship between age and gender and ischemic MR requires further investigation. The study conducted by Nixdorff et al. (8) included patients with both chronic and acute MR, therefore, the studied cohort was not homogeneous.

Lima et al. (5) compared patients with significant chronic MR and non-MR patients; local contractility abnormality of the inferior and inferior-lateral LV segments was an independent predictor of significant ischemic MR. It was concluded that this particular MI localization is the most significant for chronic ischemic MR (5), which is fairly consistent with our results. However, Lima et al. did not include in the study patients with atrial flutter/fibrillation; it explains the lack of between-group differences in LV asynergy and clinical features (5), therefore, in general, this report does not reflect the situation with chronic MR in patients with postinfarction cardiosclerosis.

There are a few literature data about the influence of coronary stenosis localization on ischemic MR; these data mainly describe the acute MR. Particularly, Nielsen et al. (9) demonstrated in the experiments that the acute ischemic MR may be caused by microembolism of the left circumflex coronary artery. Therefore, the tension of non-ischemic part of chords and MV cusps is increased; and the tension of ischemic part of anterior cusp is paradoxically decreased with subsequent relative prolapse (9). Other experimental data demon-

strate that the acute ischemic MR occurs following occlusion of exactly the proximal part of the circumflex artery, and the degree of LV systolic dysfunction does not correlate with MR (4). There are reports on significant acute ischemic MR caused by RCA stenosis (10), ligation of the left anterior descending artery (11) which reduced significantly after coronary blood flow restoration. It is known that the posterior papillary muscle is more frequently damaged by ischemia than the anterior muscle (91 versus 9%) because the latter is supplied by two coronary arteries - the left anterior descending artery and diagonal branch, and the posterior papillary muscle is supplied by one artery only -RCA or the left circumflex coronary artery (12).

In our study, significant ischemic MR was observed more frequently when RCA and obtuse marginal branch of the left coronary artery were affected; i.e. the arteries supplying the inferior-basal and inferior-lateral LV segments. However, the multivariate analysis demonstrated significant independent relationship between MR and RCA lesion only. As no significant between-group differences in the incidence of stenosis of the left circumflex coronary artery were determined; impairment of this artery probably plays no important role in the ischemic MR development. The stenosis of the diagonal branch which is observed more frequently in non-MR patients, probably indicates low significance of this artery involvement in MR development.

Of note, in the absence of significant difference in the interventricular septum thickness index and with lesser LV posterior wall thickness index in MR group, the myocardial mass index was higher in MR patients. These data combined with greater end-diastolic LV dimension suggest the eccentric type of LV hypertrophy which is typical for this population.

Interesting data on additional chords in LV were obtained: non-MR group had a tendency to its more frequent detection. It may be explained by their framework function and confirms the hypothesis that additional chords prevent abnormal LV remodeling (24).

Thus, ischemic MR in middle aged men is primarily associated particularly with the localization of coronary stenosis, i.e. RCA impairment, but not with LV global abnormal remodeling or LV asynergy. There is consistent independent relationship between MR and both the left atrium dimensions (direct), and LV ejection fraction, LV posterior wall thickness (reverse). The independent relationship between MR and total serum cholesterol level requires further investigation.

Our results indicate the importance of timely blood flow restoration in RCA during myocardial revascularization in this setting.

Conclusion

Chronic moderate-to-severe MR in middle aged men with postinfarction cardiosclerosis is associated with RCA stenoses.

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ECMO in Urgent Percutaneous Coronary Intervention in a Patient with AMI Complicated by Cardiogenic Shock

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Patients with acute myocardial infarction (AMI) complicated by cardiogenic shock have a high mortality. Although intra-aortic balloon pump is often used in patients with cardiogenic shock, it does not provide complete hemodynamic support. We report a clinical case of the use of extracorporeal membrane oxygenation for additional hemodynamic support in urgent PCI performed in patient with AMI, cardiogenic shock, and significantly unstable hemodynamics, despite of inotropic agents and intra-aortic balloon pump using.

Key words: acute myocardial infarction, cardiogenic shock, coronary stenting, extracorporeal membrane oxygenation.

List of abbreviations

- AMI acute myocardial infarction
- ECMO extracorporeal membrane oxygenation
 - VAC veno-arterial cannulation
 - VVC veno-venous cannulation
 - PCI percutaneous coronary intervention
- IABP intra-aortic balloon pump
- LBBB left bundle branch block
- RBBB right bundle branch block
- LAD left anterior descending artery
 - CA circumflex artery
 - ICU intensive care unit

Introduction

Cardiogenic shock is a critical condition associated with disturbed blood supply to organs and tissues. Cardiogenic shock is observed in 5–10% of STEMI patients and is one of the most common reasons of in-hospital mortality in this setting (1–3). Long-term survival in patients with STEMI complicated by cardiogenic shock who underwent early revascularization is higher compared to medical stabilization and delayed revascularization (4–6).

Extracorporeal membrane oxygenation is a procedure of prolonged extracorporeal circulation. It is used in patients with acute and potentially reversible respiratory, cardiac, or cardiorespiratory failure, who did not respond to

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15, Rechkunovskaya str., Novosibirsk, 630055 E-mail: Vet-007700@mail.ru Article received on June 04, 2012. Accepted for publication on June 28 2012. standard therapy (7, 8). For ECMO, membrane oxygenator is connected to a patient. There are two types of connection: veno-arterial cannulation (VAC) and veno-venous cannulation (VVC). In case of VAC, blood is collected from the veins, and then is cleaned, saturated and returned to the arterial system. VAC is recommended in newborns as well as in adults with compensated myocardial infarction. In case of VVC, blood is collected from and returned to the venous system. VVC may be used in adults with isolated pulmonary involvement. To comply with the physiological mechanisms, the blood collection and return is performed as close to the heart as possible. VAC is preferable, as the arterial blood does not mix with the venous blood. VVC requires a 2-fold larger surface of oxygenator membrane, therefore, this method is used rarely in the practice.

There is a small experience with ECMO in patients who underwent urgent percutaneous coronary intervention (PCI) for AMI complicated by cardiogenic shock or cardiac arrest.

We report a case of urgent ECMO performed in PCI Lab in a patient with AMI complicated by cardiogenic shock associated with significant hypotension, despite the use of inotropic agents and intra-aortic balloon pump (IABP).

Clinical case

A 53 year old woman has been followed-up by a cardiologist for several years with the diagnosis of: CAD, exertional angina FC II, essential hypertension, stage III, circulatory failure, class II B. During the last 6 months angina attacks occurred after walking for

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Figure 1. Parietal thrombi in LAD and CA orifices with stenoses up to 85%.

several meters. On November 25, 2011, the patient was hospitalized for urgent indications (prolonged angina attack) at the city hospital. While on treatment, the angina attacks recurred both at rest, and on small exertion. In three days the patient developed acute myocardial infarction of the anterior wall of the left ventricle subsequently complicated by cardiogenic shock (BP 85/40 mmHg; baseline BP -160/100 mmHg, HR – 143 bpm), relapsed ventricular fibrillation and transient grade III AV-block. While on treatment, chest pain repeatedly recurred, shock events persisted, AV conductivity recovered, however, complete LBBB and RBBB persisted. The patient was transferred to the Novosibirsk Research Institute of Circulation Pathology for coronarography and choice of further treatment strategy.

On admission: adynamia, skin paleness, pinched face, profuse sweating, HR = 130 bpm, brachial BP = 80/41 mmHg, moist fine bubbling rales in all parts of lungs, oliguria. ECG – atrial flutter. Blood chemistry: increased cardiospecific enzymes. Oxygen saturation (SPO2) – 78%. Acidosis. Heart ultrasound: LVEF – 22–24%. Heparin infusion was started at a dose of 1000 U/h, dobutamine – 830 µg/min, dopamine infusion at a dose of 1500 µg/min was continued; lazix 40 mg was infused intravenously and additional 60 mg.

Given the unstable hemodynamics and significant hypotension while on inotropic agents, intraaortic balloon pump was placed at the interventional radiology operating room. Coronarography was performed, which revealed parietal thrombi in LAD and CA orifices with stenosis up to 85%, chronic occlusion of the left anterior descending artery in its mid-



Figure 2. Chronic occlusion of the left anterior descending artery in its middle third.

dle third, chronic occlusion of the right coronary artery in its middle third. (Figures 1, 2, 3).

Given the acute myocardial infarction complicated by cardiogenic shock, the myocardial revascularization was absolutely indicated for this patient. Coronary artery bypass grafting might be accompanied with a very (extremely) high interventional risk. Due to increasing heart failure resistant to the high doses of cardiotonic drugs and IABP, a decision to connect ECMO and perform stenting of the affected coronary arteries was made for additional hemodynamical support.

Venous cannula 28 Fr was placed through puncture into the right femoral vein, left femoral vessels were isolated and arterial cannula 18 Fr was placed and cannula 10 Fr for blood supply of the extremity was also placed in the distal part of the femoral artery. ECMO was started: perfusion volume velocity – 4.5-4.8 L/min. The pressure in the arterial and venous lines was 280 and 90 torr, respectively.

Hemodynamics was stabilized; the doses of cardiotonic drugs were reduced. At this time V-stenting of LAD and CA was performed using the Omega stents 3.5×20 mm and 4.0×20 mm (Boston Scientific Corporation, USA) (Fig. 4, 5). The control coronarograpy revealed good angiographic results, the blood flow TIMI III (Fig. 6). The patient was transferred to the Intensive Care Unit (ICU).

During the observation and treatment at the ICU, her condition remained severe but without negative changes over time. The patient was mechanically ventilated. Acidosis was recovered.

In 8 days, following hemodynamic and respiratory parameters and acid-base balance stabilization,



Figure 3. Chronic occlusion of the right coronary artery in its middle third.



Figure 5. Stent implantation in LAD and CA.

the patient was disconnected from ECMO, IABP was removed; the patient was transferred to the cardiology department.

After rehabilitation in the cardiology department the patient was discharged home in fair condition. At discharge, LV ejection fraction was 51%.

Discussion

As the cardiogenic shock is the leading cause of death in acute myocardial infarction, the rapid and aggressive treatment plays a primary role (3, 9). Modern AMI treatment strategy primarily focuses on fastest possible revas-



Figure 4. Stent positioning in LAD and CA.



Figure 6. Final results.

cularization, however, mortality still remains very high (4, 5, 10).

Various mechanisms of circulatory support lead to reduction in mortality in this threatening complication. Thus, the SHOCK trial demonstrated reduced mortality in patients with cardiogenic shock with the use of intra-aortic balloon pump (4).

Other methods used to improve hemodynamics, include ECMO and various left ventricle bypass systems.

Although ECMO was initially developed for the treatment of patients with acute and poten-

tially reversible respiratory failure, it may be effective as an adjuvant modality in myocardial dysfunction and cardiogenic shock setting. The indications in cardiogenic shock are not ultimately established and vary at the various institutions. It is possibly due to lack of prospective, randomized, controlled studies which are difficult to be conducted ethically and practically in patients with acute disorders and high risk of death. Only a few retrospective studies and reports published in literature, in which the potential for ECMO in PCI is emphasized.

There are controversial data on urgent interventions using ECMO. Chen J.S. et al. (11) reported 7 successful cases of primary PCIs using ECMO. Although four out of these patients were successfully disconnected from ECMO already in 48 hours, in-hospital mortality was 100%. W. Tayata et al. (12) report more optimistic data. This retrospective analysis including 138 patients demonstrated improvement of inhospital and 5-year survival in patients with AMI complicated by cardiogenic shock who underwent myocardial revascularization using assisted circulation including ECMO.

Moreover, several small retrospective studies using ECMO for elective PCI in high-risk patients were conducted. According to Magovern et al. (13), ECMO assisted PCI was performed in 27 patients. This group included high-risk patients with unstable angina, congestive heart failure, and severe left ventricle dysfunction. Successful revascularization was achieved in 26 out of 27 patients (96%), including 12 patients with stenosis of the left main coronary artery. In-hospital mortality was 15% (4 patients). Causes of death were: cardiac arrest (2 patients) and heart failure (2 patients). Among the observed complications associated with this method, the authors reported relatively high incidence of complications related to the arterial access (7 patients), as well as cardiac conduction pathways block requiring pacemaker implantation in 1 patient, AMI in 2 patients and reduced cardiac output in 3 patients.

Conclusions

Therefore, ECMO may be effective in patients without previous heart failure, acute and potentially curable heart disorders, e.g. AMI complicated by cardiogenic shock.

Early ECMO use at the interventional radiology operating room in patients with AMI, cardiogenic shock and severe unstable hemodynamics resistant to inotropic agents and intraaortic balloon pump may provide additional hemodynamic support during intervention and improve prognosis in this setting.

One of the advantages of ECMO is that it may be used quickly and simultaneously with PCI.

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Peculiarities of the Clinical Course of an Acute Myocardial Infarction with Non-Occlusive Lesion of the Infarct-Related Artery (Literature Review)

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The article analyzes literature devoted to peculiarities of the clinical course of ST-elevation acute myocardial infarction with non-occlusive lesion of the infarct-related artery, detected by an urgent coronary angiography within the first hours of the disease; the article covers the problem of spontaneous reperfusion; the endogenous and exogenous factors which contribute to its development are specified, and clinical and angiographic reperfusion criteria are listed as well.

Based on the literature analysis, it has been shown that a small zone of infarction, satisfactory function of the left ventricle, a small number of complications and low both in-hospital and 6-month mortality are typical for patients with ST-elevation acute myocardial infarction and non-occlusive lesion of the infarct-related artery.

Keywords: non-occlusive lesion, spontaneous reperfusion, spontaneous recanalization, acute myocardial infarction.

List of abbreviations

- IRA infarct-related artery
- CAG coronary angiography
- CPK creatine phosphokinase
 - LV left ventricle
- AMI acute myocardial infarction
- EF ejection fraction
- PCI percutaneous coronary intervention
- ECG electrocardiography
- TIMI Thrombolysis in Myocardial Infarction (classification of the antegrade blood flow in the infarct-related artery)

Introduction

Myocardial infarction remains one of the main healthcare problems and one of the leading causes of mortality in developed countries (24). An acute occlusion of a large coronary artery causes ST-elevation acute myocardial infarction (18, 22). In 1980 DeWood M.A. et al. for the first time have proved that coronary artery thrombosis occurring in the area of atherosclerotic plaque rupture causes such occlusion in most of the cases (22). Both plateletvascular and coagulation hemostasis are involved in the development of occlusive

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thrombus. As a rule, coronary thrombosis starts with the development of unstable platelet aggregate which later on stabilizes by fibrin fibers (24).

With the lack of blood supply (including collateral) to the area of myocardium, irreversible necrotic changes begin already in 15–30 minutes and further consistently spread from subendocardium to subepicardium (wavefront phenomenon) (17, 18).

Patients with AMI and continuous occlusion of the infarct-related artery (IRA) further develop a pathologic post-infarction left ventricular remodeling – thinning and dilatation of myocardium in the area of necrosis, hypertrophy and dilatation of undamaged myocardial areas, dilatation and spherification of the left ventricular cavity (33, 42).

According to the open artery theory (E. Braunwald), an early blood flow restoration in the IRA, called an early reperfusion, limits the area of myocardial necrosis, preserves the left ventricular contractility, prevents development of post-infarction left ventricular remodeling and a number of other complications, and, as a result, decreases short- and long-term mortality rates (9, 25). The time from the pain onset to the blood flow restoration in the IRA plays a primary role in salvaging the myocardium (1, 3).

If an antegrade blood flow in the IRA is restored within the first minutes of onset of the disease, the area of necrosis is limited by subendocardium, and non-Q wave myocardial infarction develops (25). If reperfusion occurs within the first hours of the disease, a part of affected myocardium remains viable, but Qwave macro-focal or transmural myocardial infarction develops (25). If reperfusion occurs within few days of onset of the disease, salvaging of impaired myocardium is minimal; however, it reduces dilatation of the left ventricular cavity, restores electrical stability of the peri-infarct zone and improves long-term survival (25, 32, 33).

Distal embolization of microcirculatory bed by thrombotic material, which impairs the myocardial reperfusion, occurs in some patients after the blood flow restoration in the epicardial infarct-related coronary artery (24). Usually, no significant ST-segment resolution is observed on ECGs of such patients in the infarction leads. Distal embolization during the coronary angiography manifests as deceleration of the antegrade blood flow in the IRA (slow reflow phenomenon).

Currently, there are two main reperfusion strategies in the treatment of ST elevation myocardial infarction – systemic thrombolytic therapy (TL) and primary percutaneous coronary intervention (PPCI) (24). A slight risk of serious hemorrhagic complications (gastrointestinal bleedings, cerebral hemorrhage etc.) and a high incidence of incomplete blood flow restoration in the IRA are considered to be the main disadvantages of systemic thrombolysis (24). The main disadvantage of primary PCI is its limited availability, as well-equipped cath lab and trained medical staff working 24 hours a day, 7 days a week are required for its conduction (24).

In some cases of ST-elevation acute myocardial infarction, the process of complete or partial blood flow restoration in the IRA may occur without conducting systemic thrombolytic therapy or primary percutaneous coronary intervention. Non-occlusive lesion of the infarct-related artery, which corresponds to initial TIMI 2 or 3 blood flow, is observed in such patients during urgent coronary angiography (1, 2, 25, 35, 40, 41): TIMI 3 means complete and rapid antegrade filling of the IRA, TIMI 2 means its complete but slow filling (2). Such phenomenon is called a spontaneous reperfusion or spontaneous recanalization of the IRA in the literature (4, 5, 15, 20). Nevertheless, this term is disputable as, firstly, patients with STelevation AMI usually undergo antithrombotic therapy by anticoagulants and antiaggregants. and, secondly, the primary IRA occlusion was not confirmed by an angiography in most of the studies. Hence, the term non-occlusive IRA lesion will be used in this article.

In some cases reperfusion is achieved by patent collaterals, although the IRA may remain occluded (18). Schwartz H et al. have shown that in acute myocardial infarction and continuous occlusion of the IRA, collateral vessels begin to develop rapidly: well-developed collaterals are found only in 16% of patients within the first 6 hours after the myocardial infarction, in 62% of patients in 2 weeks and in 84% of patients in more than 6 weeks (23).

The incidence of non-occlusive IRA lesion in patients with *ST*-elevation acute myocardial infarction

In some cases of acute myocardial infarction, the antegrade blood flow in the infarctrelated artery is restored by endogenous mechanisms, but the time to this event may vary (minutes, hours, days) (25).

According to the data from various clinical studies, the incidence of early reperfusion in ST-elevation AMI patients significantly differs (from 4 to 30%). This differences appear to be caused by using different criteria for evaluation of reperfusion onset (clinical or angiographic) and also by different time intervals during which the assessment is conducted.

Some authors determine presence of reperfusion according to the data of urgent coronary angiography. For example, Stone G.W. et al. (1) have retrospectively studied 2507 AMI patients, enrolled in 4 PAMI trials (PAMI-1; PAMI-2; PAMI Stent Pilot, PAMI Stent Randomized Trial); non-occlusive IRA lesion was observed in 28.3% of patients who did not undergo reperfusion treatment (TIMI 3 blood flow in the IRA prior to EVP was detected in 15.7% of patients, and TIMI 2 blood flow - in 12.6%) (1). The similar data have been published by Timmis A.D. et al. (3) already in 1987: non-occlusive lesion was observed in 29% out of 41 AMI patients who underwent coronary angiography within the first 6 hours from the pain onset. During the systematic review of randomized trials, E.C. Keeley et al. (17, 18) have discovered the non-occlusive lesion of the infarct-related artery in 25-30% of ST-elevation AMI patients during urgent coronary angiography.

Other authors (Rimar D. et al., Fefer P. et al., Uriel N. et al., Ruda M.Ya. et al.) determine presence of reperfusion according to the clinical criteria; however, it is not always confirmed by the angiographic data (4, 5, 6, 7). For example, Rimar D. et al. in their study have shown that clinical reperfusion criteria were observed only in 4% out of 2382 AMI patients (5). Uriel N. et al. determined that reperfusion, established according to the clinical criteria, is confirmed in 95% of cases by urgent coronary angiography (4).

The incidence of blood flow restoration in the IRA increases over time. DeWood M.A. et al. in one of their works have shown that non-occlusive IRA lesion is observed in 13% of patients within the first 4 hours of the myocardial infarction and in 35% of patients within 12-24 hours from onset of AMI symptoms (22). It is found in approximately 50% of patients within 1 week after onset of the disease (25). In later terms (in few months after AMI), non-occlusive lesion of the infarct-related artery is also found in approximately 50% of patients (11). This is confirmed in another work by DeWood M.A. et al.; which has shown that non-occlusive lesion of the infarct-related artery was detected in 19.5% of patients within the first 6 hours of myocardial infarction, and complete occlusion was observed in 80.5% (none of patients underwent endovascular procedures); spontaneous recanalization was detected in 6 months during the control CAG in approximately 40% of patients with occluded IRA at the time of the first CAG (11).

Kreutzer M. et al. have determined that in patients older than 80 years, non-occlusive IRA lesion is observed extremely rare (34).

Mechanisms of blood flow restoration in the IRA

Investigators suggest that there are two possible mechanisms of spontaneous reperfusion (3, 9, 14):

1. Endogenous fibrinolysis leading to dissolving or recanalization of the thrombus in the infarct-related artery.

2. Termination of continuous spasm in the infarct-related artery.

Clinical signs of reperfusion

There are the following clinical criteria of reperfusion, observed not later than 6 hours after onset of the disease (3, 4, 5, 27):

1. Cessation or significant alleviation of pain syndrome.

2. ST-segment resolution greater than 50%, observed on the serial ECG, recorded at the prehospital stage and in the in-patient department prior to endovascular procedures (more than 70% according to the other authors (6, 15, 16)).

3. Early T-wave inversion in the infarction leads.

4. Accelerated idioventricular rhythm.

The first two criteria are obligatory to establish blood flow restoration in the IRA (5).

Cessation of pain by itself is an unreliable sign of reperfusion, as the pain may be ceased by opioid analgesics or partial denervation which sometimes occurs during AMI (16).

ST-segment resolution in the infarction leads is divided into complete (more than 70%), partial (30–70%) and insignificant (less than 30%) (28). ST segment resolution more than by 70% is indicative of reperfusion but is not specific enough (16). Nevertheless, complete *ST*-segment resolution in the infarction leads reflects not only IRA recanalization, but, which is more important, the blood flow restoration in the infarction area on the microcirculatory level (12, 28).

When comparing ECGs, recorded directly before and after PCI, the less marked ST-segment resolution is observed in non-occlusive IRA lesion, as compared to occlusive lesions (28). This is explained by the presence of initial STsegment resolution in patients with non-occlusive lesion even before PCI.

Accelerated idioventricular rhythm is a reliable sign of blood flow restoration in the IRA; while, other ventricular and supraventricular arrhythmias may also occur if there is no reperfusion (16).

The size of infarction zone in *ST*-segment elevation AMI and non-occlusive IRA lesion

1. Laboratory data. Elevation and further reduction of cardiac specific markers in blood (troponin I, troponin T and MB-fraction of CPK) play the primary role in the diagnosis of an acute myocardial infarction (16, 18). The degree of their elevation reflects the sizes of myocardial infarction zone. Peak concentration of CPK in non-occlusive IRA lesion is significantly smaller (which indicates a smaller area of necrosis) than during the effective thrombolysis or occluded IRA (3, 10, 19, 20, 28, 40). It is interesting that localization of infarction does not affect the degree of enzymes elevation (3).

The time to peak concentration of cardiac specific markers in blood is directly related to the time of IRA reperfusion (21). As a rule, peak CPK concentration in blood is observed at the earliest time point in patients with non-occlusive IRA lesion, at the later time point – during the effective thrombolysis, and the latest time point – in patients with occluded IRA (3).

Rimar D. et al. (5) in their study have shown that 25% of patients with initially non-occlusive IRA lesion did not develop the cardiac muscle damage at all, and they had so called aborted myocardial infarction (no significant elevation of cardiac specific enzymes and no pathological Q-wave on ECG were observed).

2. ECG data. Non-Q wave myocardial infarction is often observed in non-occlusive IRA lesions, while it is almost never observed in occlusive lesions (3, 5, 20).

Total ST-segment elevation in the infarction leads (SigmaST) on the baseline ECG in occlusive IRA lesion strongly correlates with the LV ejection fraction (the higher is SigmaST, the lesser is LV ejection fraction) (31). On the other hand, there is no such correlation in non-occlusive IRA lesion: irrespective of SigmaST value, the LV ejection fraction is insignificantly decreased (31).

The left ventricular function in non-occlusive IRA lesion

Function of the left ventricle (LV) is most completely reflected by its ejection faction, which in most cases is assessed by the left ventriculography and transthoracic echocardiography.

An early blood flow restoration in the IRA preserves LV function: it decreases the LV ejection fraction insignificantly and, as a rule, the LV ejection fraction remains higher than 55–60% (3, 13, 19, 20, 33, 37, 41).

In patients with non-occlusive IRA lesion LV ejection fraction may also slightly improve – it increases in 2 weeks, by the time of discharge from in-patient department, by 5–10% (the values are presented in absolute figures) as compared to the baseline value during the first days of disease, and it is maintained at this level till the mid-term follow-up (11, 20, 21, 41). It is interesting that improvement of ejection fraction does not depend on the localization of infarction (11). If the blood flow restoration in the IRA occurs in later terms (in 3–4 weeks after AMI), such LV function improvement usually is not observed (13).

It should be especially noted that TIMI 3 blood flow, detected by primary CAG, is associated with better LV function as compared to TIMI 2 blood flow (1, 3, 6, 10).

The state of coronary circulation in patients with non-occlusive IRA lesion

Leibowitz D. et al. have noted that in patients with initially patent IRA, its distal lesions are observed more often than in patients with initially occluded IRA (27). Dote K. et al. have shown that patients with non-occlusive IRA more often have three-vessel lesions of the coronary arteries (49%) rather than one-vessel lesions (27%) (20). Erden E.C. et al., on the other hand, have pointed out the rare incidence of multivessel coronary lesions in such patients (28).

The influence of endogenous factors on blood flow restoration in the IRA

As a rule, activity of tissue plasminogen activator (TPA), concentration of plasminogen activator inhibitor (PAI) as well as concentration of lipoprotein A in blood plasma are increased in AMI patients (25, 26).

Lipoprotein A in a high concentration may have an inhibitory effect on endogenous fibrinolysis by means of molecular mimicry (25, 29). Domains of lipoprotein A molecule are homological to domains of plasminogen; due to this fact, lipoprotein A may inhibit plasminogen in several ways: it inhibits the binding of plasminogen to endothelial cells, mononuclear leukocytes and platelets; it prevents plasminogen tissue activator from binding to plasminogen, plasminogen and plasminogen tissue activator from binding to fibrin; it blocks heparins and heparan sulfates on the surface of endothelial cells. All of these prevents endogenous fibrinolysis and promotes the growth of thrombus in the coronary artery (25).

Moliterno D.J. et al., Kim J.W. et al., Dagdelen S. et al. in their works have shown that the level of lipoprotein A in blood plasma is more than two-fold lower in patients with non-occlusive IRA lesion, as compared to IRA-occluded patients; other laboratory parameters such as concentration of serum plasminogen, plasminogen activator inhibitor, fibrinogen, cholesterol, triglycerides and lipoproteins did not differ between the groups (25, 29, 30). Thus, it has been shown that the low level of lipoprotein A in the blood serum is a predictor of the infarct-related artery patency during the acute stage of myocardial infarction (29).

High platelet reactivity and high mean platelet volume (MPV) are typical for patients with occlusive lesion of the infarct-related artery in ST-elevation acute myocardial infarction (38, 39).

Moreover, a higher white blood cell count is observed in patients with IRA occlusion at the moment of their admission to the in-patient department (39).

The influence of drug therapy on blood flow restoration in the IRA

Multiple studies have shown that antiaggregant (acetylsalicylic acid, thienopyridines, IIb/IIIa blockers) and anticoagulant (unfractionated heparin, low molecular weight heparins) therapy promotes blood flow restoration in the IRA during ST-elevation AMI (1, 2, 5, 14).

Ernst N. et al. in their work in 1702 AMI patients have shown, that antithrombotic therapy at the prehospital stage increases the incidence of IRA patency restoration from 20% up to 31% according to the data of urgent coronary angiography (2). Zijlstra F. et al. have proven that exactly the early use of aspirin and heparin at the prehospital stage increases the incidence of non-occlusive lesion in ST-elevation AMI patients by 11% (37).

Conclusions of Kreutzer M. et al. are slightly different; based on the data from Swedish Coronary Angiography and Angioplasty Register (SCAAR), they made a paradoxical conclusion that acetylsalicylic acid and clopidogrel have no effect on blood flow restoration in the IRA in *ST*elevation AMI; while heparin and IIb/IIIa blockers promote such restoration (34).

Stone G.W. et al. have proven that the incidence of initial TIMI 3 blood flow was higher in patients who received ticlopidine in addition to aspirin and heparin prior to coronary angiography, as compared to patients who received aspirin and heparin alone (20.7% against 11.3%) (1).

Skoric B. et al. have discovered that nonocclusive IRA lesion is more often observed in patients with good antiaggregant response acetylsalicylic acid (ASPI-test), and it is not observed in patients with inadequate response (36).

The GRAPE study has shown that abciximab administered 45 minutes prior to coronary angiography, effectively promotes restoration of the IRA patency: TIMI 2–3 blood flow was found in 40% of patients, more than half of them had TIMI 3 (a complete blood flow restoration) (2). Similar data with abciximab were obtained by Rakowski T. et al.: non-occlusive IRA lesion was observed in 33% of patients (35).

Furthermore, it should be noted that nonocclusive lesion is more often observed in patients chronically treated with lipid lowering drugs (34) and angiotensin-converting enzyme inhibitors (5).

Endovascular procedures in initially non-occlusive IRA lesion

Patients with non-occlusive lesion of the infarct-related artery often undergo direct artery stenting (without predilation), as most of the lesions have a low degree of residual stenosis (1, 6, 28, 35, 37). As a rule, better results are observed in such patients especially with TIMI 3 primary blood flow following endovascular procedures (1, 6, 28, 35, 37, 40).

Complications of acute myocardial infarction with non-occlusive IRA lesion

Patients with non-occlusive IRA lesion rarely develop an aneurism of the left ventricle, and due to preserved good LV function, arterial hypotension, heart failure and respiratory failure requiring respiratory support are rarely observed (1, 5, 6, 40). Due to a small incidence of complications, such patients stay less time in the in-patients department (1, 5, 6, 40).

Reinfarctions and early post-infarction angina

If residual stenosis of the target segment of the infarct-related artery persists, a high incidence of recurrent myocardial ischemia (17–34%) and reinfarctions (3%) is observed in patients who did not undergo endovascular procedures within the first hours of the disease (5, 19). Recurrent myocardial ischemia and reinfarctions are rarely observed in patients who underwent endovascular procedures on the IRA within the first hours of the disease (1, 4).

Survival and mortality

Patients with non-occlusive lesion of the infarct-related coronary artery have lower 30day mortality compared to patients who had initially occluded IRA (1, 2, 6, 10, 34, 37). Stone G.W. et al. in their work have shown that after the increase in the degree of initial TIMI blood flow, both in-hospital mortality (2.6% in TIMI 0/1; 1.5% in TIMI 2, 0.5% in TIMI 3) and 6-month mortality (4.4% in TIMI 0/1; 2.8% in TIMI 2; 0.5% in TIMI3) were significantly decreased (1). Thus, an early TIMI 3 blood flow restoration, found during the primary CAG, is a powerful and independent predictor of in-hospital and long-term survival in ST-elevation AMI patients (1, 35). Moreover, it was proven that TIMI 3 blood flow before the endovascular procedure is a more powerful predictor of survival as compared to TIMI 3 blood flow after the procedure (1).

Prognosis

Disease outcomes in ST-elevation AMI patients with non-occlusive IRA lesion (even without endovascular procedures), as a rule, are significantly higher than in patients with initially occluded IRA, who underwent primary PCI (6).

Long-term (10-year) survival is the highest for an early reperfusion (approximately 75%); while, survival rate for late reperfusion is significantly lower and according to Ishihara M. et al. data it does not significantly differ from the survival rate in persistent occlusion of the IRA (29 -55%) (13). Pitts W.R. et al. state, on the other hand, that late reperfusion (days and weeks after AMI) does not affect the left ventricular function and improves the long-term prognosis for patients due to restoration of electrical stability in the peri-infarct zone, which prevents development of ventricular tachyarrhythmias and sudden death (32, 33). The same is confirmed by Lamas G.A. et al. study which showed that cardiovascular mortality in 5 years after AMI is much higher in the group of patients with occluded IRA as compared to the group of patients who have patent IRA (23% against 12%) (33). This proves the hypothesis that nonocclusive IRA lesion improves clinical outcome irrespective of salvaging the damaged myocardium and the left ventricular function (32, 33).

Conclusions

A small zone of infarction, satisfactory function of the left ventricle, a small number of complications and low both in-hospital and 6month mortality are typical for patients with STelevation acute myocardial infarction and non occlusive lesion of the infarct-related artery, detected during urgent coronary angiography.

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Coronary Heart Disease in Patients with Diabetes Mellitus: Possibilities and Perspectives of Interventional and Surgical Treatment (Literature Review)

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To date, the studies comparing surgical and endovascular myocardial revascularization in patients with diabetes mellitus did not answer the question: "What treatment option provides significant benefits in terms of both prevention of premature death, and prevention of acute myocardial infarction (71, 93). According to World Health Organization data, the global population increased by 64% from 1995 to 2005, while the number of patients with diabetes mellitus increased by 122% (71).

Proportion of patients with diabetes mellitus will increase from 2,8% in 2000 to 4.4% in 2030 (125). Diabetes is diagnosed more often in young people (85) and children (49). Cardio-vascular mortality in these patients is 2–4-fold higher than that in the common population (46, 62). In most cases this is associated with coronary heart disease (28, 87). Thus, according to Staffieri et al. (105) in pre-insulin era, 63.8% and 18.7% patients with diabetes mellitus died from diabetic coma and cardiovascular diseases (CVDs), respectively. With introduction of insulin, mortality related to diabetic coma decreased to 3%, while CVD-related mortality increased up to 67.7%.

CHD incidence in DM patients increases with patient age. According to Dorman et al. (37), the incidence of CVDs among patients with insulin-dependent diabetes mellitus in age group over 30 y.o. is 11-fold higher than that in people of the same age without diabetes.

Diabetes mellitus is an independent risk factor for CHD progression increasing risk of this disease in 2–3 times in men and in 3–5 times in women (55). Risk of CHD occurrence in DM women in premenopause is similar to non-DM

Moscow City Center of Interventional Cardioangiology, Sverchkov per., 5, Moscow, 101000, Russia E-mail: cardiocenter@bk.ru Article received on September 16, 2012 Accepted for publication on October 18, 2012 men, as DM is considered to eliminate the protective effect of female sex hormones (23). The greater risk of CHD occurrence is explained by unfavorable influence of DM on lipoprotein levels in women (123). Coronary pathology is the main cause of death in adult patients with DM, it is approximately 3-fold higher compared to non-diabetic patients (12).

Relationship between diabetes mellitus and coronary arteries diseases

Diabetes mellitus worsens atherosclerotic process, affecting endothelial function (4, 12), diminishing reserve of coronary flow (80), increasing platelet activity (33, 110, 126), increasing fibrinogen and factor VII levels in blood (31), decreasing fibrinolytic activity (31, 64), and increasing plasminogen inhibitor level (6, 102).

Morphological investigations in patients with diabetes mellitus who died suddenly showed that atherosclerotic plaques contain more adipose cells, macrophages, and T-lymphocytes compared to suddenly died patients without diabetes mellitus (29). Even in asymptomatic patients with diabetes mellitus, stenosis of >50% is simultaneously observed in several arteries (29, 44). Moreover, in diabetes mellitus population, the main coronary arteries are affected more often and collateral vessels are affected to lesser extent (19, 108); and compensatory coronary remodeling is usually insufficiently developed (20, 82).

All above mentioned explains diffuse and distal pattern of coronary lesion in diabetes mellitus, and, as a consequence, it determines unfavorable outcome of surgical or endovascular revascularization (16, 52, 59, 116).

In patients who underwent balloon angioplasty without stenting, restenoses are observed more often in diabetes mellitus (7, 119, 120, 124). Moreover, mortality in these patients during acute phase of myocardial infarction is

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higher, and therefore, the necessity in revascularization after performed endovascular treatment is higher (3, 81). According to Billinger et al. (24) 5-year mortality in patients with diabetes mellitus was 11.4% compared to 4.3% in non-diabetic population.

Although drug-eluting stents have improved results compared to bare metal stents, nevertheless, the number of restenoses and necessity in repeated revascularization in patients with diabetes mellitus remain continuously higher than in patients without diabetes mellitus (107). According to Moussa et al. (77), the incidence of this complication was 6.9% compared to 2.9%. Diabetes mellitus is still considered obligatory to be a risk factor for all major complications related to endovascular interventions (60) including drug eluting stent thrombosis (50, 127).

In patient with coronary heart disease, myocardial revascularization decreases mortality risk within up to 5 years after treatment start (compared to drug therapy), but the results become insignificant over 5 years (42, 103).

Theoretically, coronary artery bypass grafting is more preferable, as it provides perfusion in proximal 2/3 coronary arteries, where ruptures of atherosclerotic plaques are frequently observed which result in acute coronary syndrome, while endovascular intervention is targeted to local correction of arterial obstruction, providing no protection for other atherosclerotic plaques (43). Moreover, coronary artery bypass grafting provides more complete revascularization (84). On the other hand, this surgery is accompanied with greater number of complications and prolonged hospitalization (15, 36, 66). However, diabetic nephropathy in specific group of patients decreases more significantly survival after coronary artery bypass grafting (90). Moreover, the vessel grafts (especially venous grafts) after surgery are occluded with the blood clots more frequently in patients with diabetes mellitus than in nondiabetic patients (58).

Ten-year survival after coronary artery bypass grafting (57.9%) was higher compared to balloon coronary angioplasty (45.5%). However, it was significant only for patients who underwent mammary coronary grafting using left descending artery (108, BARI trial). Two other studies (ARTS and SOS) demonstrated that CABG results were better than with using bare metal stents. Five-year mortality in CABG and bare metal stent patients was 8.3% and 13.4%, respectively (96). In another study, 6year mortality was 5.4% and 17.6%, respectively (27). The SYNTAX trial (452 patients) demonstrated that overall incidence of severe complications and deaths in patients with three-vessel disease was higher in endovascular group compared to coronary artery bypass grafting group. Thus, 1 year mortality in patients with diabetes mellitus who underwent EVI (paclitaxel-eluiting stents) and CABG was 13% and 4.5%, respectively (14).

Features of cardiovascular lesion in diabetes mellitus

Coronary atherosclerosis is the most common cause of death in patients with diabetes mellitus. According to Goto and Suzuki (45), 3151 patients with diabetes mellitus had coronary atherosclerosis as a cause of death in 41.2% cases, cerebral artery atherosclerosis – in 11.1% cases (diabetic coma was a cause of death in 4.5% cases only).

Vessel lesion related to diabetes mellitus may be non-specific (atherosclerosis and arteriosclerosis) and specific (microangiopathy). In case of atherosclerosis, the major vessels of the heart and brain are predominantly affected. The proximal part of artery is usually involved (91).

Among specific features of cardiovascular lesion in diabetes mellitus, diabetic cardiomyopathy should be noted. The typical pathomorphological changes in diabetic heart are: lymphocyte hypertrophy, interstitial fibrosis and increased glycolysation of contractive protein (18). Change in glucose level in tissues leads to endothelial dysfunction and formation of atherosclerotic plaques. Concentration of collagen and elastin is simultaneously increased, it results in dysfunction of myocardial relaxation (130). Moreover, hyperglycemia activates local renin-angiotensin-aldosteron system, resulting in cardiomyocyte necrosis (41). In parallel, metabolism of free fatty acids is affected, leading to increased atherosclerotic depot in artery walls and worsened angiogenesis (11).

Microangiopathy affects small vessels (capillaries, arteriols) and is observed in patients of all ages (75). Especially in patients with diabetes mellitus, microangiopathy induces diffuse, multifocal lesion resulting in lesser reference diameter of coronary vessels and poor development of collateral blood flow (1), it is significantly worse in terms of myocardial revascularization prognosis.

These differences manifest in clinical practice. Patients who are suffering from diabetes mellitus since youthful have predominantly diabetic microangiopathy, while the changes in large coronary vessels are predominant in patients with diabetes mellitus onset in middle and elderly age (31).

It was shown (47) that the severity of coronary lesion correlates with duration of diabetes mellitus rather than with compensation degree of carbohydrate metabolism. Normalization of glucose level with adequate blood glucose lowering therapy did not affect mortality in case of confirmed atherosclerosis (47).

Cardiac neuropathy which clearly correlates to the mortality is one of the most serious complications (neurovegetodystrophy). It develops in 22% of patients with type 2 diabetes mellitus (131) and makes misbalance of autonomic nervous system of the heart.

Features of myocardial infarction in patients with diabetes mellitus

The number of patients with diabetes mellitus among patients admitted with acute myocardial infarction has increased by 12% over 10 years (35). The overall number of admitted patients with myocardial infarction has decreased by 8% over the same period. According to Fang and Alderman (39), the number of patients with acute myocardial infarction who have increased blood glucose level, amounts to 51%. Thus, acute myocardial infarction which currently is one of the main "killers", becomes more dangerous, as it combines with diabetes mellitus increasingly (130).

In countries in which such combination has been analyzed since 1980, the number of patients with acute myocardial infarction and diabetes mellitus has increased from 10 to 24% over 15 years with 4-fold increase in highly developed countries (86).

Of course, it may be explained by both increase in the number of obese patients of "sitting" lifestyle, and improving of diabetes diagnostics (88), however, the principal alarming factor is the fact that diabetes mellitus increases mortality related to myocardial infarction in 2 times regardless of other risk factors (108).

DM patients have increased incidence of MI and acute MI has more complicated course compared to non-DM patients. Painless MI or atypical painful MI (asthmatic or abdominal type) is frequently observed in diabetes patients. It is explained by generalized dysfunction of autonomic nervous system and sensory neuropathy increasing pain threshold (9). It is quite often a reason for late diagnosis and increases a possibility of lethal outcome. Several factors affect mortality in DM patients with acute myocardial infarction. Usually, they have larger MI area, higher incidence of heart failure and shock, they also have instable metabolic status, therefore, the differences associated with insulinotherapy to prevent ketoacidosis, on the one hand, and hypoglycemia, on the other hand, arise (108). Life-threatening heart rhythm disturbances are observed in more than 25% of persons who survived 1 year after MI (108).

High incidence of heart failure (>50% of patients) is likely resulting from combination of such factors as diabetic myocardial dystrophy, lesion of both large and small coronary vessels (35).

It is widely known that acute myocardial infarction in women aged <60 y.o. is more severe and accompanied with higher mortality compared to men of the same age group (10). However, the combination of acute myocardial infarction and diabetes mellitus was frequently discovered in women younger than 55 y.o. compared to men of the same age group and is accompanied with more severe disease course (86).

Over the past decade, the number of renal diseases and hypertensia has increased. However, both diseases strictly correlate with diabetes mellitus (78).

Microangiopathy is more typical for young patients with diabetes mellitus and which is of special importance; myocardial infarction developed on this background is more severe than in older patients with atherosclerotic lesion of coronary vessels (79, 101). Brophy et al (26) reported that mortality risk associated with acute myocardial infarction or risk of repeated myocardial infarction is significantly higher in patients with diabetes mellitus especially at a young age.

Myocardial revascularization in patients with diabetes mellitus

Myocardial revascularization in patients with diabetes mellitus remains the primary problem, accounting for about 25% of all surgical and endovascular interventions for coronary heart disease (101) and relating to the worse treatment results compared to non-diabetic patients (16). This was especially recognized during the first period of bare metal stents application when long-term results were significantly worse in patients with diabetes mellitus (97). The use of drug eluting stents did not lead to significantly improved results, but the recent studies involving great number of patients with diabetes mellitus demonstrated that drug-eluting stents have certain advantages compared to bare metal stents (13, 107, 129). The incidence of repeated revascularization in patients with diabetes mellitus is high (regardless from the previous intervention: coronary artery bypass grafting or endovascular intervention) (122). The reason for it is the fact that diabetes mellitus leads to increased atherothrombotic risk (89) stimulating coagulation and changing prothrombotic status. Revascularization does not eliminate diabetes mellitus although stenting reduces restenosis and thrombosis (95) not eliminating it. The atherothrombosis mechanisms inducing remain unchanged and, as a consequence, repeated in-stent thrombosis was observed more often (97).

Thus, two processes – underlying disease progression (diabetes mellitus) and restenosis lead to repeated revascularization. In turn, they are stimulated by hyperglycemia (73). Hyperglycemia induces endothelial dysfunction, primarily, due to enhanced formation of free radicals (115), decreased prostacyclin level (118), and dyslipidemia (21).

Immediate angiographic success of stenting in patients with diabetes mellitus is 92–100%, it is comparable with the results in non-diabetic patients (8, 25). The incidence of peri-interventional mortality, non-fatal myocardial infarction and urgent repeated interventions varies approximately from 0.7 to 6.75%; it does not differ from the incidence of these complications in non-diabetic patients (2, 38). However, the prognosis in insulin-dependent diabetes is worse. Abizaid et al. (2) determined that perioperative mortality in patients with insulin dependent diabetes mellitus is 2% compared to insulinindependent diabetes mellitus (0%) and nondiabetic patients (0.3%).

The long-term results in patients with diabetes mellitus are significantly worse after both endovascular and surgical (CABG) interventions compared to non-diabetic patients (2, 38, 106).

Moreover, the incidence of occlusion in patients receiving insulinotherapy was 2-fold higher compared to patients not receiving insulin (119). Some authors explain this fact with more significant neointimal hyperplasia in patients with insulin-dependent DM (12, 17, 53).

The long-term results of EVI in patients with diabetes mellitus are significantly worse com-

pared to non-diabetic patients: restenosis rate in DM is 24–40%, while this parameter in nondiabetic patients is 20–27% (25, 38).

Drug-eluting stents (DES) allowed to reduce restenosis incidence by 70–80%. (30, 38, 52, 74, 92, 106).

RAVEL, SIRIUS, TAXUS II, and TAXUS IV trials compared drug-eluting stents (sirolimus and paclitaxel) and bare-metal stents (BMS) in patients with diabetes mellitus. Significant reduction of restenosis rate in patients with diabetes mellitus was observed when DES containing sirolimus were used compared to BMS (6.9% and 22.3%, respectively, p < 0.001) (76). With drug-eluting stents, significant reduction of restenoses rate by 70–80% was observed.

Moreover, significant reduction of restenosis rate in patients with diabetes mellitus was reported with drug-eluting stents used for extended lesions (>15 mm) and small vessels (<2.5 mm) (5, 61).

Above mentioned data are almost similar to the primary results from the ongoing studies SECURE (60, 114, 2).

Restenosis in diabetes mellitus

Cutlip et al. (34) reported that diabetes mellitus is a predictor for restenosis increasing its incidence within 1 year after EVI by 50% compared to non-diabetic patients. Restenosis rate in patients with diabetes mellitus is still quite high accounting for 24–40% (2, 38, 106, 121).

Arterial remodeling and acute overstretching of vessel wall caused by balloon angioplasty induce neointimal proliferation, which, in turn, leads to restenosis of vessel lumen (51, 67, 68). The mechanisms inducing post stenting restenoses include inflammation resulting in chronic constrictive remodeling; allergy to metal frame of the stent; intimal protrusion between stent struts (40, 53, 54).

Increased restenosis rate in patients with diabetes mellitus is related to more intensive intimal hyperplasia (53). In diabetes mellitus, high collagen level is observed in vascular wall, it provokes fibrin production and intimal hyperproliferation after elastic overstretching caused by balloon angioplasty.

However, the mechanisms of restenoses in patients with CHD and DM after endovascular procedures are not well understood. It is hypothesized that increased blood levels of growth factors with chemical structure similar to insulin, and insulin itself, may promote smooth cell proliferation and intensive formation of extracellular protein matrix for hyperplastic intima (12). On the other hand, histological examination demonstrated that the basis of restenosis substrate is a fibrous extracellular substance but not smooth cells (72). This would indicate that the primary mechanism of restenosis in MD patients after endovascular procedures is fibrous "shrinkage" of vascular lumen.

Vessel restenosis often leads to long-term occlusion resulting in decreased left ventricle ejection fraction (119) and increases mortality in patients with diabetes mellitus after balloon angioplasty (120).

In-stent stenosis in diabetes mellitus is caused by greater rigidity, neointimal hyperprolifiration and matrix deformation (69).

Metabolic and functional disorders in vascular endothelium related to DM, induce vasospasm, increase vascular thrombosis risk (98, 112) and lead to increased tendency of vascular thrombosis due to depression of fibrinolytic activity of the blood (83, 102). Additionally, insulin influences on intimal hyperplasia, increases smooth cell migration and proliferation and extracellular matrix production (3, 109).

Predictors for restenosis

in diabetes mellitus

The completed studies reported that restenosis rate after interventions in small vessels (<3 mm) in patients with diabetes mellitus is 40-70% (56, 111).

Microalbuminuria is one of the risk factor for restenosis after EVI. Heper et al. (48) in the study involving 159 patients with diabetes mellitus, determined that microalbuminuria increases restenosis rate after interventions.

Hyperinsulinemia and impaired glucose tolerance in diabetes mellitus also have unfavorable effect on the results of interventions (25). The interaction between these factors increases restenosis (117) and vascular thrombosis risk (99).

Prevention of restenosis in diabetes mellitus

Currently, it is commonly recognized that active measures targeting risk factors for cardiovascular complications significantly reduces restenosis after endovascular interventions in non-diabetic patients but also in patients with diabetes mellitus (110).

One of the effective prophylactic measures to prevent restenosis in diabetes mellitus is a tight glycemic control. Corpus et al. (32) have proved significant reduction in restenosis rate in patients with tight glycemic control compared to patients without adequate blood sugar control. This is due to the fact that in the lack of adequate glycemic control, blood level of glycosilated hemoglobin increases (>7% of the total hemoglobin), it is one of the predictor factors for restenosis. Other investigators obtained the similar results (65, 70).

In addition to glycemia and blood lipid control in diabetes mellitus, blood pressure has an important role in prevention of restenosis. Blood pressure in patients with diabetes mellitus should not exceed 130/80 mm Hg (128).

New medicinal products affecting receptors which increase glucose intake by adipocytes and skeletal myocytes are currently being investigated. The products of this group include thiazolidinedione, roziglitazone, and pioglitazone. These drugs in vitro inhibit smooth cell proliferation and decrease postinterventional restenosis; however, application of these drugs is still limited due their high hepatotoxicity (57, 113).

The use of IIb/IIIa receptor blockers reduce 30-day mortality after endovascular interventions in patients with diabetes mellitus by 40% (22). Based on meta-analysis of completed randomized, placebo-controlled studies of the efficacy of IIb/IIIa receptor blockers, Roffi et al., (94) concluded that these drugs decrease intervention-related mortality from 6.2% to 4.6%.

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Coronary Heart Disease in Patients with Diabetes Mellitus: Possibilities and Perspectives of Interventional and Surgical Treatment

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